lume 42 Number 10

The JOURNAL

OF THE MICHIGAN STATE MEDICAL SOCIETY

On the beautiful Au Sable River at Grayling, Michigan, where all is quiet and at peace in a world at war.

Complete Contents on Page 795

CTOBER 1943

Single Copies 50 Cents
Yearly Subscriptio
$5.00

Wyeth's Phosphaljel is supplied in 12-fluidounce bottles*

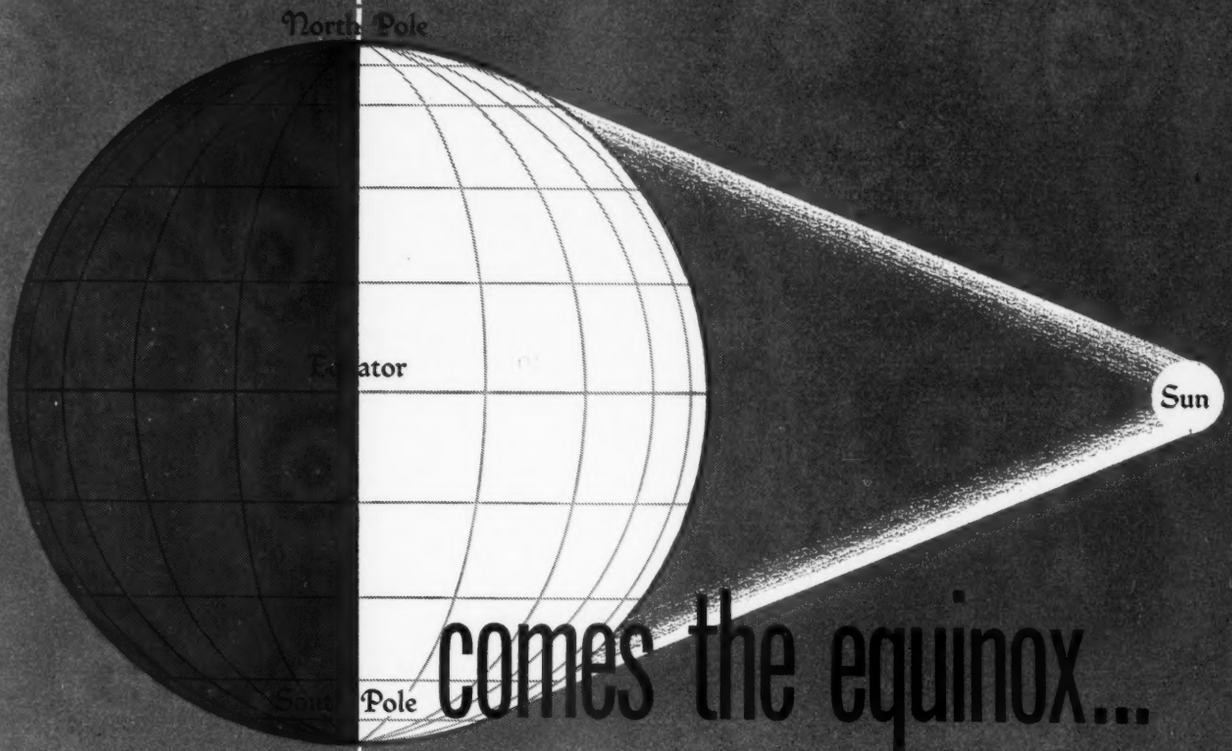
PHOSPHALJEL WYETH'S ALUMINUM PHOSPHATE GEL

Effective in the treatment of gastrojejunal ulcer and other cases of peptic ulcer associated with a relative or an absolute deficiency of pancreatic juice, diarrhea, or a low phosphorus diet.

*Reg. U. S. Pat. Off.

Phosphaljel contains 4% aluminum phosphate.

JOHN WYETH & BROTHER • INCORPORATED • PHILADELPHIA



comes the equinox...

and with the change of season comes an increased need for the vitamins of cod liver which are provided in

White's cod liver oil concentrate

White's Cod Liver Oil Concentrate presents the *natural* vitamins A and D derived only from cod liver oil itself—in the proportions found in U.S.P. cod liver oil.

Free from excess fatty oils and bulk, it provides three pleasant, simple dosage forms for prescribing the A and D vitamins of cod liver oil for your various patients—infants, growing children, adults:

Liquid—for drop dosage to infants.

Tablets—pleasantly flavored—children may chew them.

Capsules—where larger dosage is indicated.

Economical—In contrast to the high current retail cost of plain cod liver oil, White's Cod Liver Oil Concentrate provides potency at an economical price. Prophylactic antirachitic dosage for infants costs less than a penny per day.

Ethically promoted—not advertised to the laity. White Laboratories, Inc., Pharmaceutical Manufacturers, Newark 7, N. J.

ACCEPTED AMERICAN MEDICAL ASSN.

White's PRESCRIPTION *vitamins*

EDITORS COMMENT

UNCLE SAM, M.D.

Awaiting consideration by the present Congress is a bill of revolutionary social consequences and it calls for utmost scrutiny throughout the land as well as on Capitol Hill. It would enable the federalization of the study and practice of medicine, a radical departure from our tradition and the system under which the Nation has enjoyed the fruits of voluntary regulation, education and research free from political control and personal discretion in the choice of physicians and hospitals. And there are approved types of medical and hospital assurance for those who wish such protection.

Senator Robert F. Wagner of New York and Senator James E. Murray of Montana are the sponsors and after two readings it was referred to the Finance Committee. The bill is labeled with the general purpose of broadening the Social Security Act and it has the meritorious objective of bringing within its benefits certain classifications not now included. The definition given the proposal by the senators might catch one off guard with such purposes as "to alleviate the economic hazards of old age, premature death, disability, sickness, unemployment and dependency . . . to extend the coverage, and to protect and extend the social security rights of individuals in the military service," etc. But one goes on and finds this clause: "to establish a Federal system of medical and hospitalization benefits; to encourage and aid the advancement of knowledge and skill in the provision of health services and in the prevention of sickness, disability, and premature death."

Directed by the surgeon general of the United States would be a richly financed program controlling the practice of medicine and this could be extended to virtually complete coverage of the field; rules prescribed by him would determine the latitude of the public in the choice of doctors and hospitals; compensation to the profession might be on a fee, per capita or salary basis; maximum number of individuals served by each physician could be regulated or available patients distributed pro rata among available physicians.

The bill provides for a study and recommendations for the extension of this service to include "dental, nursing and other needed benefits," a report to be made not later than two years after enactment.

Subsidy and therefore virtual control of medical education would result, the bill authorizing the surgeon general "to administer grants-in-aid to nonprofit institutions engaged in research or in undergraduate or postgraduate medical education" and there is specific provision of funds for such purposes.

This is one of the more questionable aspects of the proposal. It is another of the attempts toward Federal control of education through "the back door."

Financing would come through a boost in social security taxes. Instead of one per cent as now, employes would pay six per cent on income up to $3,000 a year and employers would contribute six instead of four per cent. Under certain conditions, Federal, State and municipal employes would pay a tax of 3½ per cent. It is estimated this would increase the annual revenue to $12,000,000,000, a fourth of which would be credited to "the medical care and hospitalization account" to cover the costs of the new program. With such a sum, after $600,000,000 for administrative costs, there would be enough to pay each of the 120,000 physicians now available for civilian practice $5,000 each per year; to buy every available bed in every nongovernment owned hospital at $5 per day, 365 days per year; to pay $2.50 per day for each government owned hospital bed, 365 days per year; and have $181,565,887.50 left for drugs and medicines.

Under the bill there could be $48,000,000 available for medical education and research which is sufficient to meet the total operating costs of the country's 66 accredited medical colleges, subsidize the average of 22,000 medical students at $700 each per year with a residue of $11,108,752 for research.

Federalized medical education and research, practice and hospitalization smacks of something foreign to the way of life for which we are fighting.—*The Flint Journal,* August 15, 1943.

(Continued on Page 778)

(Continued from Page 776)

THE LEGION HAS BEEN MISINFORMED

Doctors of Michigan were startled a few days ago by the publicity given a Michigan American Legion resolution to blacklist physicians who refused to comply with the government's proposed method of rendering maternity and child care to families of servicemen.

To clear the record let us repeat that the medical profession favors the granting of necessary funds directly to the wives of men in the armed forces, and has raised an objection only as to the method of payment. The misunderstanding is in regard to the *application* of federal monies allocated, and the Legion appears to be purposely misinformed and is perhaps being used as a cat's paw. Under the guise of a war measure, certain federal bureaucrats are attempting to Europeanize both service families and the medical profession.

Our profession yields to no one in its recognition of its obligations to the serviceman and his family. We feel that the wives of our soldiers and sailors should have a *direct and all inclusive* maternity benefit available to them to compensate for the sacrifices they and their husbands are making. If, then, it should ever happen that they are unable to meet their medical expenses there isn't a doctor in Michigan or elsewhere who would not render the necessary medical services without thought of recompense. Ours is a group that has rendered, is rendering, and will continue to render, service to all on both the war and home fronts.

With all due respect, the American Legion has no corner on patriotism.—STANLEY W. INSLEY, in *Detroit Medical News*, August 30, 1943.

OBSTETRIC CARE FOR WIVES OF SERVICE MEN

The President has approved H.R. 2935, making appropriations for the Department of Labor, the Federal Security Agency and related independent agencies for the fiscal year 1944. This law appropriates $4,400,000 for grants to states, including Alaska, Hawaii, Puerto Rico, and the District of Columbia, "to provide, in addition to similar services otherwise available, medical, nursing, and hospital maternity and infant care for wives and infants of enlisted men in the armed forces of the United States, under allotments by the Secretary of Labor and plans developed and administered by state health agencies and approved by the Chief of the Children's Bureau."

As reported to the House, June 14, H.R. 2935 carried the following proviso to the title of the bill making appropriations for the Department of Labor:

"Provided, that no part of any appropriation contained in this title shall be used to promulgate or carry out any instruction, order, or regulation which discriminates between persons licensed under state law to practice obstetrics."

The Senate Committee on Appropriations, on June 24, recommended that the proviso be stricken from the bill. Thereafter, the Senate acquiesced in the recommendation of its committee and passed the bill June 29. A conference committee then considered the bill and agreed to recommend that the proviso be reinserted with the following additional phraseology:

"Provided further, that the foregoing proviso shall not be so construed as to prevent any patient from having the services of any practitioner of her own choice, paid for out of this fund, so long as state laws are complied with."

The conference report was considered in the Senate on July 2. There was no vote specifically on the recommendation of the conferees in connection with the proviso in question, but an effort was made to induce the Senate to reject the conference report because of that recommendation. The vote in the Senate was on the adoption of the conference report as a whole. Senator La Follette of Wisconsin, Senator Lodge of Massachusetts, Senator Chandler of Kentucky, Senator Hill of Alabama, Senator Maloney of Connecticut and Senator McClellan of Arkansas argued for the rejection of the conference report because of the recommendation it contained with respect to the proviso. Senator La Follette remarked, in part, as follows:

"Mr. President, I say that to yield on this matter is a step backward in modern practice of obstetrics, and it is unfair to the servicemen, who are preparing to give their lives for their country, if necessary, that their wives, who are pregnant, and who are to be delivered in their absence, shall not have the benefit of the finest standards and the finest care that money can procure.

"Yet in this false application of the so-called

(Continued on Page 780)

(Continued from Page 778)

doctrine of states' rights such a situation will be created that the Congress will have done that very thing. So far as I am concerned, Mr. President, I want no part of it. I want no father of a child born while the father is overseas fighting for his country to point his finger at me and say, 'You are responsible for the death of my wife and child in my absence, because a man was permitted to minister to her at her time of need who was not properly equipped, who was not licensed to use drugs, who was not licensed to practice surgery.'

"Mr. President, I say such a thing would be an outrage."

After considerable discussion, the Senate voted to adopt the conference report by a vote of 42 to 32, with 22 Senators not voting. **Michigan's two Senators, Vandenberg and Ferguson, voted against the conference report with its objectionable amendment, and merit the thanks of the medical profession and particularly the people they tried to protect.**

As the bill was approved by the President, therefore, it contains the following proviso in the title relating to appropriations for the Department of Labor:

"*Provided,* that no part of any appropriation contained in this title shall be used to promulgate or carry out any instruction, order, or regulation relating to the care of obstetrical cases which discriminates between persons licensed under state law to practice obstetrics: *Provided further,* that the foregoing proviso shall not be so construed as to prevent any patient from having the services of any practitioner of her own choice, paid for out of this fund, so long as state laws are complied with."—*Wisconsin Medical Journal,* September, 1943.

MATERNITY AND INFANT CARE IN OHIO

An emergency maternity and infant care program for the wives and children of enlisted men of the armed forces, based on the rules and regulations laid down by the United States Children's Bureau, is now in effect in Ohio. * * *

It will be up to each physician to decide for himself whether he wishes to accept patients under the plan. * * *

The program does not have the endorsement of the Ohio State Medical Association which is on record as opposing it on the basis of principle and for specific reasons which were set forth in a Statement of Policy.

When the Scripps-Howard Newspapers decided to make this question a political issue, and an excuse to point the finger of criticism at the present state administration, obviously the Army Emergency Relief and Red Cross became jittery, as they cannot afford to be drawn into a political wrangle. When the pressure was put on at Washington to get them to take a hands-off policy, they politely had to state that they could carry on no activity which would in any way supplant the Children's Bureau proposal. When certain newspapers saw to it that little, if any, of the Association's side of the question reached the reading public, the attitude of the Association was not understood and false impressions were acquired by some citizens.

The Association re-learned a valuable lesson: The time to exert efforts to stop the spread of governmental medicine is while proposed legislation is pending and before the measure authorizing any proposal such as that of the Children's Bureau is enacted into law.

We believed then we could have arranged a program which would have produced much more satisfactory results than the proposal of the Children's Bureau. However, we have been prevented from following through with our sincere intentions because certain interests have seen fit to make this a political issue and because pressure has been exerted to keep certain voluntary agencies from negotiating with us on this matter.

We are convinced that the proper way to provide necessary financial aid to the families of servicemen for medical care is through stated cash grants, specifically for medical care and paid directly to such families by the government or voluntary agency assuming the responsibilities. That is the method which is being used to assist such families in obtaining other necessities. It is our intention to offer this recommendation for consideration by the Congress.

It has been intimated that the medical profession has been unpatriotic because it has disagreed with the Children's Bureau. The patriotism of the physicians of Ohio does not need to be defended. It is well known and is evidenced by contributions which physicians have made and are making to the war effort.—*Ohio State Medical Journal,* September, 1943.

NOT HOW FAST ...*but,* HOW LONG

THE CHOICE of a sedative for the sleepless patient is not alone dependent upon the rapidity of its action, but also upon the duration of action and how the patient feels when he awakens.

Ipral Calcium—a moderately long-acting barbiturate—induces a sound restful sleep closely resembling the normal. One or two tablets, administered orally approximately one hour before sleep is desired, provides a six- to eight-hour sleep from which the patient awakens generally calm and refreshed.

Ipral Calcium is a plain white tablet—and one not easily identified by the patient. It is readily absorbed and rapidly eliminated and undesirable cumulative effects may be avoided by proper regulation of dosage.

HOW SUPPLIED

Ipral Calcium (calcium ethylisopropylbarbiturate) in 2-grain tablets and in powder form for use as a sedative and hypnotic. ¾-grain tablets for mild sedative effect throughout the day.

Ipral Sodium (sodium ethylisopropylbarbiturate) in 4-grain tablets for pre-anesthetic medication.

Elixir Ipral Sodium in pint bottles.

For literature address the Professional Service Dept., 745 Fifth Avenue, New York 22, N. Y.

E·R·SQUIBB & SONS, NEW YORK
MANUFACTURING CHEMISTS TO THE MEDICAL PROFESSION SINCE 1858

CORPORATIONS CANNOT PRACTICE DENTISTRY OR MEDICINE

A corporation cannot practice dentistry and cannot, by employing licensed dentists, offer such services to the public or to its employes as part of the compensation and benefit of such employment, either for a fee or gratuitously. The same principle applies to physicians, except when they perform emergency service in factories. Physicians cannot conduct the general practice of medicine in such first-aid departments.

This syllabus is based on the July 1, 1943, opinion of Michigan's Attorney General Herbert J. Rushton. The complete text of the Attorney General's opinion follows:

Does the State Dental Law permit employment by industrial establishments of full time or part time dentists for diagnostic or remedial service, and if so does it make any difference if such dental services are provided on a nonprofit basis to the corporation?

In answer to this question reference should be made to various provisions of the Dental Act, Act No. 122 of the Public Acts of 1939. Such pertinent provisions of the Act are as follows:

"Sec. 15. No corporation shall practice or continue to practice, offer or undertake to practice or hold itself out or continue to hold itself out, as practicing dentistry. Every person practicing dentistry as an employe of another shall cause his name to be conspicuously displayed and kept in a conspicuous place at the entrance of the place where such practice is conducted: Provided, however, That nothing herein contained shall prohibit a licensed dentist from practicing dentistry as the agent or employe of any charitable institution or hospital.

"Sec. 12. A person practices dentistry, within the meaning of this act, when it shall be shown:

"2. That he is a manager, proprietor, operator or conductor of a place where dental operations are performed; or

"3. That he performs dental operations of any kind gratuitously or for a fee, gift, compensation or reward, paid either to himself or to another person or agency; or ***"

"Section 14. The terms 'manager,' 'proprietor,' 'operator' or 'conductor' as used in this act shall be deemed to include any person:

"2. Who places in the possession of an operator, assistant or other agent such dental material or equipment as may be necessary for the management of a dental office on the basis of a lease or any other agreement for compensation for the use of such material, equipment or office; or

"3. Who retains the ownership or control of dental material, equipment or office and makes the same available in any manner for use by operators, assistants or other agents: Provided, however, That the above shall not apply to bona fide sales of dental material or equipment."

Section 18 provides several causes for the revocation or suspension of the license to practice dentistry. Subsections 5 and 6 of Section 18 read as follows:

"5. For conducting the practice of dentistry so as to permit directly or indirectly an unlicensed person to perform work which under this act can legally be done only by persons licensed to practice dentistry or oral hygiene in this state;

"6. For practicing dentistry under a corporate, assumed, trade or firm name in violation of the provisions of this act;"

Section 21 is also important for this section reads:

"Sec. 21. This act shall be deemed to be passed in the interests of the public health, safety and welfare of the people of the state and its provisions shall be liberally construed to carry out its object and purposes."

From the foregoing it is clear that there is no question but that a corporation cannot practice dentistry and that a corporation cannot by employing licensed dentists offer such services to the public. It follows that such corporation cannot offer such dental services to its employes as part of the compensation and benefits of such employment. Nor does it matter that such services may be given gratuitously by the corporation to the employes for the practice of dentistry is defined as including such gratuitous dental practice.

The restriction on dental practice also extends to the dentist himself for the proviso in Section 15 indicates that a dentist may be employed only by another dentist or a charitable institution or hospital for the purpose of performing dental services to the public. The purpose of this provision seems to be to maintain professional control of such dental practice in the hands of a

(Continued on Page 784)

CORPORATIONS CANNOT PRACTICE MEDICINE OR DENTISTRY

(Continued from Page 782)

licensed dentist. This principle is supported in the case of People vs. Carroll, 274 Michigan, Page 451, where the Court on page 456 says:

"It is a well known fact that in the profession of dentistry the services rendered are personal and call for knowledge in a high degree and that to separate this knowledge from the power of control is an evil, the correction of which was attempted by the instant legislation. The evils which arise from divorcing the 'power of control' from 'knowledge' apply with equal force to a partnership as well as a corporation."

It is obvious that where a corporation employs a dentist the control and responsibility for such dental practice would lie with the corporation and this is what the legislature apparently sought to avoid.

It is assumed that the question does not relate to an arrangement whereby the dentist is employed by the establishment to perform dental services for an employe in his own office where he has unlimited and full control, full and exclusive use, and management of such office and equipment. Such arrangement would not conflict with the provisions of the act.

Re the employment by a corporation of physicians in their first-aid departments: the same principle applies to physicians except that physicians in so performing medical services at factories perform emergency service. Physicians cannot conduct the general practice of medicine in such first-aid departments. The Medical Act provides for emergency treatment as an exception to the provisions of the Act. The Dental Act does not provide for emergency treatment as such exception for the reason that the legislature probably felt that there could be no emergency need for dental services.

Following World War I, the French records show that in German occupied France deaths from tuberculosis were 3.3 per 1,000 before the war. From 1916-17 they rose to 5.75 per 1,000. However, tuberculosis increased in all other countries during and after World War I, including the United States. The death rate was so alarming, especially in France and Germany, that the attention of our people was directed toward it, resulting in surveys and aid in various ways. C. M. Hendricks, Col. MCR, Diseases of the Chest Jour., May-June, 1943.

WAR BULLETINS

NAVY DISCOVERS SERUM TO COMBAT INFLUENZA

A serum which, when vaporized and inhaled into the lungs, has successfully combated influenza and will make impossible a repetition of the disastrous 1918 epidemic, has been discovered by Navy research men under the direction of Commander Albert Paul Krueger (MC) USNR, John Moreland discloses in *Collier's Weekly,* August 27, 1943.

"We need no longer fear an influenza epidemic," says Moreland, who states that Commander Krueger "is the man chiefly responsible for the discovery" which "rivals such classics of medical research as the work of Koch and Pasteur."

The Navy is building up an enormous stockpile of the serum which established drug concerns, also may manufacture for sale to the general public.

Commander Krueger, head of Naval Laboratory Research Unit No. 1, and stationed at the University of California in Berkeley, was assigned in 1942 to study methods for the prevention and treatment of influenza. Complex and innumerable experiments followed before results were achieved.

As long as any of the serum, inhaled in mist form, remains in the lung tissues it neutralizes influenza virus breathed in by a patient and protects him against the disease, writes Moreland who adds:

"Animal experiments have proved this protection to be 90 per cent effective for immunization. Even after the disease has been contracted, experiments indicate, the new agent will cure 50 per cent of cases.

"So far, the human experiments have been conducted with an inhalation apparatus which consists of a cylinder containing the atomized serum, connected by rubber hoses to oxygen masks. A dozen men can be treated at one time by this method."

POSTWAR MEDICAL ECONOMICS

In the postwar period the physician will be confronted with two major functions. Enjoying, as he almost invariably does, the respect of his community, it will be his duty to utilize his understanding of human psychology to assume leadership in movements which set the pace for good government and citizenship. He will render a service to his country if through precept and example he will influence those with whom he associates to emulate a well-balanced philosophy of life.

The second function is a corollary to the first. It relates to his professional and economic safeguard through a policy of frankness and sincerity on the dangers of bureaucratic schemes applied to medical practice. From sources as variable as they are questionable, many a man on the street has heard so much about "free medical care" that he has accepted the idea as a promise on face value. Though he knows nothing about its implications he is willing to indulge in the delusion that some mysterious agency in the person of a rich uncle, will cheerfully and eagerly finance his medical bills. To counteract the medical-economic propaganda barrage which is now stirring the public mind the individual physician must in the interest of preserving the prevailing high standards of American Medicine accustom himself to discuss with his patients whenever the opportunity warrants it, the problems which medicine faces; and dispassionately interpret the advantages of the present methods over those promulgated by theorists and politicians.—Editorial, *Nebraska State Medical Journal,* July, 1943.

INDUCTION OF PHYSICIANS AND DENTISTS

1. Authority has been granted to waive the age limitations for induction in the cases of physicians and dentists between the ages of 38 and 44 inclusive, who are declared available for military service by the War Manpower Commission's Procurement and Assignment Service for Physicians, when such waivers are requested by a State Director of Selective Service.

2. When such a waiver is granted, letter will be written by this Headquarters to the State Director of Selective Service concerned, advising him of the fact that age limitation has been waived and that registrant may be forwarded for induction. Notices will be furnished State Directors in quintuplicate and, in order that identical distribution may be effected, one copy will be attached to each copy of the DSS Form 221 at such time as registrants are delivered for induction.

3. Registrants of this category will be included on induction reports and reports of rejections the same as in the case of all other registrants. The only deviation from normal procedure will be that this class of registrants will be listed by name on the reverse side of Daily Report of Inductions, with notation as to whether they were accepted or rejected.

By Command of Major General Aurand

MEDICAL EDUCATION FACILITIES FULLY MEETING WARTIME NEEDS

The Council on Medical Education and Hospitals, of the American Medical Association in its forty-third annual report published in the *Journal AMA,* August 14, says the number of doctors excellently trained, being graduated is the largest in history.

The report states that the accelerated medical education program and increased enrolments in medical schools "are now producing excellently trained medical graduates for military and civilian needs in numbers far exceeding the production of doctors at any time in the history of this country. . . ."

Not only are the medical schools of the nation prop-

(Continued on Page 788)

WAR BULLETINS

(Continued from Page 786)

erly handling the increased enrolments, but improvements in curriculum also are being inaugurated. "Practically all schools," the report says, "report that, while the basic medical curriculum remains essentially unchanged, subjects of war significance are being stressed or have been added. The most commonly mentioned subjects in this category are Tropical Medicine and Parasitology, First Aid, Shock and Blood Substitutes, Burns and War Wounds, Venereal Diseases, Aviation Physiology and Medicine, Industrial Medicine, Public Health, Chemical Warfare, Military Medicine and Chemotherapy.

"Two generalizations may be made from scanning this list: First, the subjects are not limited to clinical topics of a purely 'practical' nature but involve as well material of basic scientific importance. Second, many of these subjects will continue to be of great medical importance after the war, so that these wartime additions to the curriculum are not simply necessary educational concessions to an emergency but will probably continue to justify their inclusion in our educational programs after the war. . . ."

The increased demands on medical schools are being met by faculties seriously depleted by the numbers who have entered the armed forces. Up to July 1, 1943, the seventy-six medical schools and schools of basic medical sciences in the United States had contributed 5,637 faculty members to the armed forces.

"Acceleration in medical schools does not involve any basic change except the elimination of the long summer vacations. A significant increase in weekly work by the student is not required. The premedical programs, however, shorten the program mainly by a weekly increase in the quantity of work carried by the student. . . .

"Whether or not students will be able to carry this heavy load remains to be seen. These students will, however, be free from financial worries and the necessity for outside employment. They will receive medical care, and more attention will be paid to the students' physical condition.

"The results of this experiment in concentrated premedical education will be watched with interest by all who are concerned with the preprofessional education in every field, since it may offer a solution of the problem of reducing the long years of training required by the learned and scientific professions. . . ."

Postwar medical educational facilities are not being ignored. The *Journal AMA* says that "Recognizing that large numbers of physicians will be seeking advanced training immediately after the war, the Council on Medical Education and Hospitals is making a careful study of the educational facilities in the graduate and postgraduate fields. A preliminary survey has already been instituted to determine what institutions and agencies will be able to expand their regular educational activities to meet additional postwar needs. . . .The large number of physicians who return to civilian life will likewise find that the medical profession, the schools and the hospitals stand ready to meet the educational needs of the postwar period."

MENINGITIS DEATH RATE NOW LESS THAN 3.5 PER CENT

In a series of 1,518 cases of meningococcic meningitis and septicemia in the Army's Fourth Service Command during the winter and spring of 1942-1943, an early mortality rate of 8.8 per cent in 317 cases was lowered during February and March to 2.1 per cent in 761 cases, Colonel Henry M. Thomas, Jr., reports in *The Journal of the American Medical Association* for October 2.

Colonel Thomas says that this "amazing reduction in mortality from 39 per cent in the last war to less than 3.5 per cent in the present war is due entirely to chemotherapy (drug treatment). It is true that the most desperately ill patients may require additional therapeutic measures but for over 95 per cent of all patients chemotherapy properly administered is the only specific form of treatment necessary.

"Of the various sulfonamide compounds sulfadiazine has up to the present proved to be the most satisfactory in the treatment of meningococcic infections. It is more efficatious than sulfanilamide, and with one important exception it is much less toxic than sulfapyridine and sulfathiazole. . . . If all patients could be given a diagnosis and treated at the onset of the first symptom, it is my firm belief that the mortality would be reduced to zero. However, the disease is often masked by the absence of pathognomonic symptoms (on which a diagnosis can be made) and by the simultaneous occurrence of many infections of the upper respiratory tract presenting similar symptoms. This leads inevitably to loss of time in treatment in a few cases. In other cases the infection is so virulent that the patient dies before treatment can be given or before treatment has an opportunity to stem the tide of infection. . . ."

As for prevention, Colonel Thomas says that "the feasibility and effectiveness of large-scale prophylactic use of sulfadiazine in the reduction of carriers and the prevention of cases are being demonstrated. It has been possible then to compensate by improved methods of treatment and prophylaxis for the rapid training program which necessitated fatigue, exposure and crowding of unseasoned troops. It seems safe to prophesy that in succeeding years the case rate can be greatly reduced by prompt prophylactic treatment at suitable points, particularly among unseasoned troops. It seems equally safe to prophesy that the mortality from the cases that do develop will be held to low levels, although the occasional cases of fulminating disease probably will continue to produce a small number of deaths."

The JOURNAL
of the Michigan State Medical Society
ISSUED MONTHLY UNDER THE DIRECTION OF THE COUNCIL
VOLUME 42 OCTOBER, 1943 NUMBER 10

The Skin in Endocrinology*

By Carleton J. Marinus, M.D., M.Sc.
Detroit, Michigan

M.D., 1921, University of Michigan, Assistant Professor of Clinical Medicine, Wayne University.

A discussion of common skin disorders from the viewpoint of the Endocrinologist. Alopecia areata temporarily benefited by thyroid treatment. No permanent benefit. Improvement in the quality of the hair in myxedema with appropriate treatment. No benefit from endocrine therapy in the common vertex type of baldness. Mechanism of male type of hair growth in males and females is discussed. Stimulation of male hair by androgenic therapy. No effective therapy for excess or abnormal hair growth in women unless associated with ovarian tumor. Treatment then surgical. Acne vulgaris due to excess androgenic as compared with estrogenic hormones. Suggestions for treatment. Senile atrophy of the skin and Androgens. A certain group of cases of eczema associated with relative excessive pituitary function as compared to ovarian function.

■ THE modern dermatologist is interested in the etiology of the lesions coming to his attention. Many times he suspects that there may be a glandular disturbance responsible for the pathology before his eyes. This idea has been fostered by numerous reports in the literature indicating that certain skin lesions respond to endocrine therapy. If one attempts to guide his treatment by the procedures advised he is frequently, if not usually, disappointed by the results obtained. Out of the confusion in the literature and out of my own observations covering fifteen years of endocrine practice, I hope to outline certain basic conceptions and clarify to some extent the possibilities of endocrine therapy in dermatology.

*Read at the seventy-seventh annual meeting of the Michigan State Medical Society, Grand Rapids, September 25, 1942.

For purposes of simplification, we might consider in turn, disorders of the appendages, the hair and nails, disorders of vascular supply, and disorders of the skin itself.

The mechanisms controlling hair growth are unknown. It is felt that hair growth is, in part at least, controlled by a hormone or hormones produced by some gland of internal secretion. What this hormone is or where it is produced, we do not know. We see luxurious hair growth before the onset of puberty and after sex activity is past. During the period of sex life there is a difference in hair growth, both in quality and distribution. This would indicate that the sex glands play a part in the nutrition of the hair follicles.

Failure of hair growth, alopecia, is frequently ascribed to endocrine deficiency. Results of treatment are disappointing. In alopecia areata there is frequently a re-growth of hair in the bald spots following the administration of thyroid extract. If treatment is continued the condition recurs; new bald spots appear which are not improved by changing the thyroid dosage. We must conclude that the effect of thyroid in these cases is nonspecific and that the alopecia is not the direct result of thyroid deficiency. Complete alopecia is not affected by thyroid in any dosage.

Thinning of the outer third of the eyebrows is quoted as a diagnostic sign of thyroid deficiency. The administration of thyroid does not result in the reëstablishing of hair in these areas. In true myxedema, on the other hand, one sees a characteristic disturbance in hair growth in that all of the hair is lifeless, brittle, dull in color, and falls out easily. With the administration of thyroid there may be a complete loss of all the old hair followed by the development of a new crop which is luxurious, deeper in color, elastic, and strong.

If, however, the case is of long standing before treatment is initiated, one may find that the hair follicles are atrophic and do not regain their function.

By far the most common types of hair loss is the vertex baldness seen in males and apparently of hereditary origin. This appears most commonly at forty but may occur very early in life and is limited to the scalp. The pubic, body, axillary hair, and beard are normal or may be unusually luxuriant. This same type of baldness occasionally appears in women. I have never seen improvement in this type of baldness by any form of endocrine therapy, including the pituitary therapy so strongly advocated a few years ago.

With failure of development of the sex glands in the male, there is a failure of development of hair in the masculine distribution, beard, chest, pubic area, et cetera. Growth of hair in these areas may be stimulated by activation of the quiescent sex gland by gonadotrophic therapy, or by direct administration of the male sex hormone. Loss of the male sex hormone by castration or disease results in gradual diminution of hair growth in the masculine areas. This can be reactivated by administration of the appropriate hormone.

One of the problems of the dermatologist is the appearance of hair growth in the masculine distribution in women. Extreme examples are seen in cases of tumor of the suprarenal, pituitary, and ovary. Ablation of the tumor results in gradual disappearance of the abnormal hair. Because of these observations it has been postulated that milder degrees of abnormal hair growth are due to disorder in one of these three glands. Administration of glandular extracts is singularly ineffective in treating these cases.

How can one correlate the observations which I have sketchily outlined above into a simple, clear concept which would be of value in determining treatment? First, the thyroid hormone is necessary for the normal function of the hair follicles just as it is necessary for the normal function of all the other cells of the body. In the presence of a marked thyroid deficiency there is definite impairment of the nutrition of the hair follicles resulting in colorless, lifeless, brittle hair. This is generalized and affects equally the hair follicles throughout the body. The presence of such generalized disturbance in hair growth would indicate the advisability of a metabolism test and the response to adequate thyroid treatment will be good. Local disturbances in follicular activity, such as in alopecia areata or typical baldness, cannot be due to thyroid deficiency and do not respond to treatment.

Hair growth in the masculine areas requires the presence of the male sex hormone. Certain quantities of this hormone are present in females as well as males. When the quantity of the male hormone is deficient in the male there is a lack of hair growth in the masculine areas, in the presence of normal growth on the scalp. Growth of hair in the masculine areas may be stimulated by appropriate therapy.

When hair growth is seen in the masculine areas in women, the problem is more complex. We are dealing here with a lack of balance between the male and female hormones with a relative or absolute excess of the male hormone. The excess production of male hormone in the female results in a general masculization. There is amenorrhea, loss of the feminine type of fat, change in muscle contour approaching the male type, change in voice, change in personality, as well as change in the hair distribution. The abnormal hair growth is luxuriant and progressively increases in quantity. This picture should inevitably suggest new growth which may be found in the ovary, the suprarenal or the pituitary gland. It is required that the tumor be located and removed because of the possibility of malignancy. Early diagnosis may be life-saving. Complete removal of the offending tissue restores the patient to her previous normal.

The majority of cases of excess hair growth in the masculine areas in women are due to a relative deficiency of the female hormone without excess production of the male. In these cases, one may see minor disturbances in menstruation and other evidences of deficient ovarian activity. One would expect that the adequate administration of female hormone would correct the imbalance, normalize menstruation, and control the abnormal hair growth. I have followed this line of treatment in a large group of cases with the following results. When theelin is administered in sufficient quantities to bring about a therapeutic result the patient's production of theelin is interfered with, the cyclic character of the menstruation is altered, and the patient's general condition is impaired. Persistent treatment does result in decreased vitality of the abnormal hair, reaching a point where the hair can be broken off

at skin level by simple rubbing and its rate of growth so slowed that it is no longer apparent. Promptly upon the cessation of treatment the hair growth starts in again and may be even more luxuriant than before treatment was started.

The mechanism of this result is as follows: with the administration of therapeutic doses of theelin the gonadotrophic activity of the pituitary gland is inhibited and the ovaries go into a resting stage in which there is no activity. The endometrium no longer undergoes the cyclic changes. When treatment is suspended the pituitary regains its gonadotrophic function and ovarian activity and the resultant endometrial changes return. The level of the gonadotrophic activity may not reach the level that was present before therapy. I believe this program of treatment to be definitely harmful and definitely contra-indicated.

An alternate method of treatment is an attempt to increase ovarian activity and thereby increase the production of female hormone by gonadotrophic therapy. There are a number of gonadotrophic materials on the market. Some are derived directly from the pituitary gland; others are obtained from the urine of pregnant women. During the adolescent period the urinary gonadotropins, of which Antuitrin S. is an example, are effective in stimulating ovarian development, resulting in increased ovarian activity. After the adolescent period, the response of the ovaries to this type of stimulation is strikingly decreased.

I have a large series of adult cases in which Antuitrin S. was given in large dosages over a prolonged period of time. In the majority of cases there has been no satisfactory evidence of increased ovarian activity either in the character or rhythm of menstruation or in the abnormal hair growth. There is an occasional case in which relatively small quantities of Antuitrin S., given shortly before the expected time of ovulation, have resulted in normalization of the menstrual cycle. In these cases, the amount of abnormal hair growth has not increased and the pigmentation and stiffness of the hair has decreased. In no case has the abnormal hair growth entirely disappeared.

The gonadotrophic hormone derived from the anterior lobe of the pituitary itself would theoretically be more appropriate in these cases. This hormone is either a protein, or so closely linked to a protein, that these materials have a strong antigenic activity. The use of these materials hypodermically frequently results in severe local reactions and may produce a generalized anaphylaxis. Their use is not without danger. It is often impossible to continue treatment long enough to produce the desired therapeutic result.

As a result of these experiences, I have reached the following conclusions: When an adult patient presents herself with abnormal hair growth as the major symptom, without other important disturbances in function, I do not treat her with the glandular products. When the patient's major complaints indicate the need for endocrine therapy, I will accept her for treatment and will expect to see some improvement in the abnormal hair growth, but do not expect restoration to normal.

The endocrinologist frequently sees alterations in the nails of his endocrine patients. Brittleness, flaking, longitudinal and transverse ridging are common complaints. Transverse ridges are indicative of temporary nutritional changes and cannot be due to a chronic metabolic disturbance. Longitudinal ridges are seen in numerous conditions; thyroid deficiency, nutritional disorders, and vitamin deficiencies. These symptoms are nonspecific and indicative of chronic disturbance in cellular nutrition. In severe deficiency of the anterior lobe of the pituitary, such as is seen in pituitary dwarfism, Simmond's Disease, et cetera, the nails are smooth, thin, and hyper-flexible. In thyroid deficiency, the nail is thick, grows slowly and is brittle. It may or may not be ridged. In recent years we have seen excessive flaking or splitting of the nails. This is not an endocrine disorder, but is the direct result of the use of paint and its appropriate solvents upon the nails.

Vascular disturbances of the skin are extremely common in endocrinology. The most common, of course, are the hot flashes associated with the natural or artificial menopause. These are amenable to estrogenic therapy, using either the natural hormone or the synthetic Diethylstilbestrol. In nearly every case of hot flashes we find an opposite reaction; namely, vaso-constriction, involving usually the extremities. The vaso-constriction also responds to estrogenic therapy. In these cases the problem of impairment of the patient's own theelin production is unimportant as the patient is rapidly approaching the time when her own ovarian activity will spontaneously cease.

One frequently finds in younger women a syn-

drome of vascular instability identical with, but less severe than, that observed at the menopause. In these cases the phase of the vaso-constriction may be more disturbing than the vaso-dilatation. The vaso-constriction may be so great as to result in trophic disorders in the skin, nails, or joints of the hands, even approaching a true Reynaud's Disease. In most of these cases one will find other evidences of impaired gonadal activity such as eunuchoid body proportions, unstable emotional reactions, et cetera. If the case is recognized before the age of twenty or twenty-five, ovarian activity may be increased by appropriate gonadotrophic therapy, resulting in a true cure. If the ovaries do not respond to this stimulation, the symptoms may be kept in control by the use of the crude ovarian extracts. It is rarely necessary to use theelin and, if used at all, the dose should be small, 1,000 to 2,000 units, two or three times a month.

Trophic disorders in the skin may result from long-continued, severe endocrine disturbances. The skin of thyroid deficiency has been described as dry and scurfy. The classic example is the thick, dry skin of the cretin. This type of skin is seen only in severe thyroid deficiency of long standing. There is an actual atrophy of the sweat glands and the sebaceous glands, and occasionally of the hair follicles. The skin itself is thickened because of deposits of mucin. There is a curious translucence giving the "alabaster" quality. This skin is to be differentiated from other dystrophic disturbances such as congenital ectodermic defect, ichthyosis, and in adults, the skin associated with leukemia, et cetera. Under thyoid treatment, the skin becomes thinner, soft and pliable, but the atrophied structures are not replaced.

The skin undergoes a change during sexual maturing with the production of an increased amount of sebaceous material. This is apparently due to the male hormone rather than to the female hormone. If sexual maturing is delayed as in pituitary deficiency the adolescent skin will retain the characteristics of pre-adult state. If sexual maturing is induced by adequate gonadotrophic therapy, the activity of the sebaceous glands is increased.

In the adult eunuch this characteristic increased sebaceous activity can be produced at will by the administration of the male hormone. The administration of the female hormone does not result in increased sebaceous activity. In these respects, those skin conditions associated with excessive activity of the sebaceous glands will be considered as in the same classification as, and due to the same mechanism, as are increases in hair growth in the masculine areas. Clinically, it is very common to see abnormal hair growth associated with overactivity of the sebaceous glands.

The basic mechanism underlying acne vulgaris, whether appearing at puberty or later in life, is therefore intimately associated with the male sex hormone and its quantitative relationship to the female sex hormone. Severe acne in the adolescent male is usually associated with unusually rapid sexual maturing. It is therefore self-limited, but during the period of its activity may be sufficiently severe to produce permanent scarring. I do not believe it should be treated by the endocrinologist because I can see no logical reason for decreasing sex function to give a better complexion. Local therapy is certainly indicated.

In the female, excessive acne indicates no real excess of the male hormone but a relative deficiency of the female hormone. This indicates glandular imbalance. If the menstrual periods are regular and of normal quantity and duration, it is probable that the imbalance is temporary and will correct itself. In these cases therapy should be local until time demonstrates that the disturbance is not self-limited.

If the menstrual periods are abnormal, and particularly if the body proportions are those of eunuchoidism—relatively long extremities, poorly developed breasts, or obesity—the case should have endocrine therapy. In this group, as in the cases of abnormal hair growth, the most spectacular results are obtained by the use of theelin. This type of therapy is of but temporary benefit and may impair the already poor pituitary function. In my opinion, ovarian therapy is distinctly contra-indicated in this group.

Gonadotrophic therapy has been advised in acne since the report of Lawrence about five years ago. The results of treatment have been reported as varying from about 90 per cent cures to about 90 per cent failure. This wide discrepancy in results is difficult to interpret.

The earlier reports covered the use of urinary gonadotropins such as Antuitrin S. This material has a distinct value in stimulating ovarian maturation if given during the adolescent period. It is rarely effective in the adult. It has no direct effect upon the acne. One criterion of adequate

dosage is the establishment of a normal cyclic menstruation. If this result is obtained, there will be a corresponding improvement in the acne. If normal menstruation is not obtained, the acne will not be benefited.

At the present time we have available a gonadotrophic material consisting of the gonadotrophic hormone derived from the anterior lobe of the pituitary fortified by the addition of urinary gonadotropin. This is marketed under the name of Synapoidin, Parke, Davis & Co. My number of cases treated with this material is relatively small but it seems to be more effective than the older materials. Here again, the criterion of successful treatment is the establishment of normal menstruation. When this is accomplished, the acne progressively improves. If menstruation again becomes abnormal, the acne will be worse. With continued normal menstruation one can be assured that the acne will eventually clear up. There should be sufficient local therapy to prevent scarring.

With advancing age and the appearance of general senility one frequently sees trophic changes in the skin. Such trophic changes are occasionally seen in younger individuals with other senile manifestations. Recent observations on the administration of male hormone for the relief of the functional disturbances associated with the male climacteric and milder degrees of prostatism, indicate an improvement in the skin following its use. The skin becomes thicker, less dry and wrinkled, and there is a definite relief of "winter pruritus." Small amounts of male hormone may be used with advantage, therefore, in the thin, dry, itchy skin seen in elderly people whether male or female. This may be applied as an ointment or as the methyl ester of the hormone by mouth. The quantity needed is small and the results are extremely gratifying to the patient.

I wish to mention briefly two rare disturbances in the skin which seem to have an endocrine basis. A recent report states that the lesions of pemphigus can be caused to regress or recur by the administration or withholding of that fraction of suprarenal cortex which controls salt metabolism.

I have seen three cases of scleroderma in which the long continued administration of crude anterior lobe pituitary has resulted in regression of the skin defect and eventual restoration to normal.

Finally, we come to eczema. I wish to state categorically that I do not consider eczema to be an endocrine disease. There are certain types of patients, however, in whom an endocrine imbalance is a factor in the eczema. I think most dermatologists will agree that eczema is the expression of various interacting factors and that there may be several disorders included in the single classification. Thus, in infantile eczema the factor of allergic sensitization to one or more foods seems to be the outstanding etiology. One may see in older individuals the development of an eczematous state following exposure to simple irritants, to proven allergens, or to injudicious local medication. In these cases the removal of the offending food or local allergen may be sufficient to bring about a cure.

In the majority of cases of eczema, the problem is not so simple. If one studies, from an endocrine standpoint, a group of patients suffering from eczema he finds one type which occurs with sufficient frequency to have apparent significance. These are girls in the adolescent or early adult age period who show a rather masculine type of body build with coarse features, prominent lower jaw, and bulky, boney framework. The facial bones are suggestive of the acromegalic type. These patients are physically active and have good endurance. They are mentally above the average. They present a complex problem from the emotional standpoint. There is a definite feeling of inferiority which the patient frequently ascribes to her unattractive skin. They are inclined to be timid and retiring, frequently depressed, but unable to express their feelings.

In these cases the menstrual periods are usually somewhat late in appearing, tend to be delayed or irregular, are frequently painful, and may be either profuse or scant. To make it more confusing, in some of these girls the menstrual periods are perfectly normal.

There is usually a definite instability of the vasomotor system with excessive flushing on emotion, reddening of the chest, blotchiness of the skin generally, and cold extremities. There is often a seborrhoic disturbance involving the face, chest, and scalp. There is frequently a complaint of mal-odorous perspiration.

From the endocrine standpoint these cases would be diagnosed as representing a dysfunction of the pituitary with excessive production of the growth hormone and a deficiency of the gonado-

trophic hormones. The dermatologic history in these cases may go back to infancy, at a time when the endocrine diagnosis could not be made. It is more common to find, however, that the eczema began or became more severe with the onset of adolescent changes at the age of ten or twelve. There are certain features regarding the eczema which suggest its endocrine basis. There is very commonly a marked exacerbation of the eczema under two conditions; first, during the week or ten days before each menstrual period and second, explosions of increased exzematous activity during and following emotional stress. In a large proportion of these cases one can also find an allergic factor in foods so that the ingestion of certain foods will precipitate an exacerbation of the eczema.

Animal research has demonstrated a definite antagonism between the growth hormone and the gonadotrophic hormones of the pituitary. It would therefore seem logical to treat these cases with gonadotrophic materials. Unfortunately, this line of attack is unsatisfactory as the majority of these cases prove hyper-sensitive to the extracts, developing large, red, hot swellings at the points of injection. If treatment is continued in spite of local reactions no benefit is derived.

If one treats these cases with the older crude ovarian products, one obtains very satisfactory results. The pre-menstrual exacerbation can be prevented completely if the dosage is adequate. There is a definite stabilization of the emotional reactions as a whole so that the patient is less likely to develop an eczematous flare-up as the result of emotional experiences. There is even a decrease in the allergic response of the skin to the specific food substances to which the patient may be sensitive.

In the majority of the cases, fifteen to thirty grains of a potent desiccated whole ovarian preparation given daily in divided doses after meals will be adequate to maintain control except under unusual circumstances. In the more severe cases it may be necessary to use whole ovarian substance, one or two c.c. subcutaneously, two or three times a week during the pre-menstrual phase. Occasionally, I may need to use theelin, two thousand units subcutaneously, two or three times during the inter-menstrual cycle.

In order to demonstrate that these results were not psycho-therapy, I have repeatedly substituted capsules of beef muscle, which have an identical appearance, for the ovarian capsules. In each instance there has been a prompt recurrence of the eczema. I frankly admit that I always advise concurrent local therapy in the beginning to expedite control. In the case that is to respond, I know that endocrine treatment and avoidance of the allergenic foods will result in relief, but only after a period of time. With local therapy the results are much more prompt.

This form of treatment is not curative in the sense that it decreases the patient's primary endocrine imbalance. It is purely substitution and must be continued until the patient has passed the need for it. It does afford a means of controlling the chronic eczemas which fall into this classification. I should emphasize that this program has not been successful in the treatment of girls with slender bones, strikingly feminine features, et cetra, who do not present the endocrine picture described above. One should not consider, therefore, that all cases of eczema should be treated with ovarian therapy.

I have presented several dermatologic conditions which I have successfully treated as an endocrinologist. How would one approach a dermatologic problem from the endocrine standpoint? The case should be studied as an endocrine case. Complete history, including a family history of possible endocrine disturbances, is the first step. A series of measurements to determine body proportions and possible deviations from normal relationship is the next step. Finally, laboratory work including metabolism tests and x-rays of the sella turcica and of the epiphyses. Quantitative determinations of the hormones in the blood and urine will eventually prove of great value but have not at present reached a point of certainty in making a diagnosis. Finally, the use of a therapeutic test with control of the positive results by the use of inert placebos will confirm the diagnosis.

Case 1.—Mrs. C., aged fifty-three. Myxedema for duration of fifteen years. Basal metabolic rate—42 per cent. Hair scant, thin, brittle, dull gray, of normal distribution. Following the administration of thyroid extract, grains V daily (gradual increase in dosage over a period of three months), there was a loss of all the hair on the body and scalp. Immediately following this a new crop of hair of normal distribution appeared. The new hair grew rapidly, was coal black in color, glossy, elastic, and somewhat coarse. During a period of several years of continued treatment the

hair gradually turned gray and finally nearly white but still maintains its good texture.

Case 2.—Mr. H. Eunuch, aged twenty-five. This patient did not develop sexually because of a severe pseudo-Froelich syndrome at puberty. When seen at twenty-five he had lost the abnormal obesity but was fatigued, emotionally unstable and suffered from vertex headaches. The genitalia were the size of an eight-year-old boy's. There was no pubic, axillary, or body hair. He had never shaved. The scalp hair was abundant, fine, and elastic. One-thousand units of Antuitrin S. were given subcutaneously three times weekly for six months. At this time the testicles were three-quarter inches in the longest diameter and definite epidydimi were palpable. The penis measured two and one-half inches when flaccid and four and one-quarter inches when erect. There was abundant, fine lanugo over the body and some axillary hair. It was necessary to shave twice weekly. At this point testosterone, twenty-five milligrams subcutaneously twice weekly, was started. There was continued growth of the penis and the beard required shaving daily.

Case 3.—Miss O., aged thirty-five. Cushing's syndrome. Amenorrhea of three years' duration, gain of 30 pounds in weight, deepening of the voice. This girl shaved twice weekly, there was complete absence of hair on the vertex, with coarse black hair on the rest of the scalp. There was marked excess hair on the legs and arms. The pubic hair was strikingly triangular in distribution. Various kinds of glandular therapy were given without success.

Case 4.—Mrs. M., aged twenty-five. Functional hypogonadism. Acne and excessive hair growth. Acne began at puberty; excessive hair growth during the past five years. Periods irregular, patient fatigued, hyper-emotional, eunuchoid body proportions. Antuitrin S., 750 units two weeks before period due. When the injection is taken period comes on time, there is no acne, and symptoms are relieved. When the injection is omitted or a placebo substituted the period is late and the acne occurs as severely as if no therapy had ever been used. During a year on this program the facial hair growth has become lighter in color and the individual hairs finer. The hair grows just as rapidly but no new hair has developed.

Case 5.—Miss L., aged fourteen. Eczema began at the elbows and knees at the age of six years. Marked increase involving the face and neck at twelve. Increase in severity one week before each period but never entirely clear. Menses began at twelve, five week intervals, profuse. Extreme dermatographia, masculine features, malocclusion treated with dental bands. With ovarian substance by mouth the pre-menstrual exacerbation controlled. Hypodermic ovarian substance required during emotional stress, at examination time, et cetera. While on this program no eczema occurred except after indulgence in foods to which the patient is sensitive. Treatment discontinued after six years with no recurrence.

The Place of Hormone Assays in Clinical Medicine*

By Gardner M. Riley, Ph.D.
Ann Arbor, Michigan

A. B., St. Stephen's College, 1931; M.S., 1934, and Ph.D., 1936, State University of Iowa. Research Associate in Endocrinology, State University of Iowa, 1936-39; Assistant Physiologist, Beltsville Research Center, U. S. Department of Agriculture, 1939-42; Endocrinologist and Instructor in Obstetrics and Gynecology, University of Michigan, 1942.

Various hormone assays being used in clinical medicine are discussed and certain claims concerning their usefulness in differential diagnosis are evaluated. Quantitative determinations of urinary chorionic gonadotropin (modified Aschheim-Zondek test) are useful in detecting the presence of an hydatid mole or chorioepithelioma and are of prognostic value in cases of testicular teratoma. Tests for pituitary follicle-stimulating gonadotropin are considered of significance only in marked hypo- or hypergonadism. Estrogen determinations are useful in determining the presence of feminizing tumors of the ovary; 17 ketosteroid values are helpful in determining the cause of virilism; and pregnandiol determinations may be used as a gauge of corpus luteum function.

■ It is becoming increasingly evident that the endocrine laboratory qualified to perform certain routine biological tests and hormone assays can offer an invaluable service to clinicians. An outstanding example of this is the widely used biological test for pregnancy, the clinical significance of which is well recognized.

With the rapid growth of endocrinology certain other tests have been suggested as useful aids in both diagnosis and prognosis. Many of these tests have not been generally available to practitioners and even when the services of a laboratory could be obtained the expense to the patient has made the use of such facilities prohibitive. In some respects this is fortunate since frequently the determinations have been of doubtful significance and the interpretations often misleading. With continued progress and the lapse of sufficient time for more critical evaluation, certain tests and assays are becoming accepted as useful diagnostic aids.

It is the purpose of this report to point out briefly some of the hormone assays that are

*Read at the seventy-seventh annual meeting of the Michigan State Medical Society, Grand Rapids, September 25, 1942. From the Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, Michigan.

being used in clinical medicine today and to evaluate certain claims concerning their usefulness in differential diagnosis. In general, these tests consist of qualitative or quantitative determinations of substances of endocrine origin excreted in the urine.

Chorionic Gonadotropin

During pregnancy a gonadotropic substance is excreted which is entirely different from any which are found in normal nonpregnant women. This substance is only found in the presence of living chorionic tissue and is called "chorionic gonadotropin" or anterior pituitary-like (A.P.L.) hormone. The appearance of this substance is the basis for the widely used pregnancy tests (Aschheim-Zondek or Friedman) based upon gonadal stimulation in the experimental animal. As far as accuracy of results are concerned it seems to make little difference which test is employed. Aschheim[1] claims 98 per cent positive diagnostic results with the mouse test in 925 normal pregnancies; and 99.5 per cent negative results in 1,075 nonpregnant control women. The majority of reports show the rabbit test to give correct positive reactions for pregnancy in 97-100 per cent of cases.

The high degree of accuracy obtained in these tests is in large part due to the specificity of the physiological effects of this gonadotropin; two characteristic effects being (a) luteinization of atretic follicles and (b) intrafollicular hemorrhage ("blood-spots").

Since large amounts of chorionic gonadotropin are elaborated by the chorionic tissue of the hydatid mole and by chorio-epithelioma we find here a special field of usefulness. Quantitative Aschheim-Zondek tests may be useful in detecting the existence of these abnormal growths. It was earlier thought that very high values for chorionic gonadotropin were diagnostic for these growths.[11,25] It is now clear that a single high value cannot be accepted as conclusive evidence. High values are also found during a brief period in early pregnancy, several hundred thousand rat units being sometimes found from twenty to fifty days after the first missed period.[10] However, after the third month, a high chorionic gonadotropin titre may be accepted as strong evidence of these pathological conditions. Furthermore, if the values do not show a decrease in repeated monthly tests it is highly probable that a tumor is present.

The finding of values equivalent to those characteristic for the greater part of pregnancy does not rule out the presence of chorionic tumor or hydatid mole since low values and even occasional negative tests have been found in the presence of either of these conditions.[15] In such a circumstance a single biological test affords very little aid in diagnosis. The detection of chorio-epithelioma after the removal of an hydatid mole by quantitative determinations of chorionic gonadotropin is occasionally complicated by either unusual and unexplainable persistence of gonadotropin excretion or by the possibility of an intervening pregnancy. Payne has recently expressed the view[24] that if, following molar evacuation, regularly space quantitative tests are made for six months to a year, it is possible to definitely differentiate between recovery and the development of chorio-epithelioma. There is little doubt but that repeated assays after the removal of a mole or chorio-epithelioma would lead to early recognition of incompleteness of evacuation.

Chorionic gonadotropin is also found in the urine in the presence of testicular teratoma. The amounts of the gonadotropin excreted have been found to vary from a hundred rat units or less per liter of urine to as much as one million rat units. A positive test for chorionic gonadotropin in a case of tumor of the testis can be accepted as diagnostic evidence of the malignancy of the growth. On the other hand a negative Aschheim-Zondek test does not rule out the possibility of a teratoma being present. Successive assays at regular intervals postoperatively are useful in determining the existence of metastases and as a guide to therapy.

Anterior Pituitary Gonadotropin

During the reproductive years relatively small amounts of anterior pituitary gonadotropic substances are excreted in the urine of men and women. In women the excretion of gonadotropin is low throughout the menstrual cycle but there is usually a cyclic appearance of increased amounts. The peak of excretion occurs most frequently near the middle of the cycle[7,13,18] and has been associated by some authors with the occurrence of ovulation.[6,21] However, the fact that Heller has recently reported multiple peaks

in some cycles would seem to minimize the importance of the urinary gonadotropin peak as an indication of ovulation. In addition to the variability in the number of peaks Heller also finds great variability with respect to their time of appearance and magnitude. This author considers it "unlikely that urinary gonadotropin determinations will be of any clinical diagnostic value except in the extremes of gonadal dysfunction."

It is well established that increased amounts of pituitary follicle-stimulating hormone (FSH) are excreted in the absence of ovarian function. Thus, following menopause and surgical castration or in amenorrhea due to ovarian failure, increased amounts of FSH are found in the blood and urine.[12,34] Tests for FSH can be of some use in determining whether the pituitary or ovary is at fault in cases of amenorrhea. In the event of pituitary failure little or no gonadotropin will be excreted, whereas, if the ovaries are at fault this substance will usually be found. The results of the test will therefore give some indication of the therapeutic treatment required. Since even in oöphorectomized women gonadotropin excretion fluctuates from day to day, one should not draw conclusions from a single gonadotropic test.

We are using in our laboratory a rather simple procedure for gauging pituitary gonadotropin function. The dried alcohol precipitate from 100 c.c. of a first voided morning specimen of urine is dissolved in tenth normal sodium bicarbonate and injected into four three-weeks-old mice so that each animal receives the equivalent of 25 c.c. of urine. A negative result may mean one of two things: the pituitary is either functioning normally or its activity is less than normal. Additional tests using larger amounts of urine would be necessary to determine which of the two conditions existed. On the other hand, if a positive response is obtained it is a definite indication of hyperpituitary activity, which in turn, points to extreme hypoövarianism.

Estrogen Assays

Equipped with an understanding of the normal estrogen excretion rates we should be able to use estrogen assays as an aid in the diagnosis of ovarian dysfunction. The early recognition of the excretion of abnormally large amounts of estrogens in pregnancy led to the use of estrogen assays as a satisfactory biological test for pregnancy. This test, though popular at one time, has been virtually replaced by the gonadal stimulation tests.

There are numerous instances where it would appear that estrogen assays would be of clinical use. Thus, in the case of many of the common ovarian dysfunctions it would be of some value to know the extent and nature of ovarian function. It should be remembered, however, that due to wide variations in normal estrogen excretion—during the cycle as well as between individuals—several successive assays must be made before any diagnostic value can be attached to such determinations.

Due to our still incomplete understanding of the mechanism of menstruation, even thorough investigations of the estrogen excretion are of doubtful value at present. Frank's study of blood and urine estrogen levels in amenorrheic patients revealed at least three groups—one with absent or greatly diminished secretion and excretion, another with normal estrogenic concentrations and a third in which the secretion and excretion were greatly increased. These differences make even a theoretical consideration of the underlying causes of amenorrhea difficult.

Large amounts of estrogen have been found in the urine of patients with ovarian tumors of the feminizing type, particularly granulosa cell tumor. The finding of continuous, high estrogenic titres is strong evidence of the presence of a granulosa cell tumor.

Occasionally this type of tumor occurs in children before the age of puberty resulting in precocious development of the secondary sexual characters. Estrogen assays would have some differential diagnostic value in those cases where the age of the patient or the absence of characteristic symptoms rendered the diagnosis difficult.

In view of laborious procedures involved in estrogen assays and their doubtful clinical value it is suggested that other diagnostic methods be relied upon. In most instances hyper- or hypoestrinization can be detected by a thorough physical examination supplemented with endometrial biopsies or the examination of vaginal smears.

Androgen Assays

Except during pregnancy when the concentration of estrogens in the urine is very high, biological assays for estrogenic activity must be employed. Within recent years, however, labora-

tories interested in androgen (male sex hormone) excretion in the human have used a colorimetric method introduced by Zimmerman[33] and further developed by others.[4,32] This method is based upon a color reaction which is produced when certain ketosteroid substances unite with metadinitrobenzene. To these substances Callow and associates gave the name 17-ketosteroids.

This colorimetric test does not distinguish between substances having androgenic activity and those which do not. For this reason values obtained with colorimetric methods are usually higher than those obtained by such biologic methods as the capon comb test. Since under normal and most abnormal conditions the androgens contribute the greater part of the chromogenic property of urinary extracts, Callow and associates were of the opinion that there is a significant correlation between the results obtained from biologic tests and from colorimetric determinations. Most other workers have accepted this view. Values are usually expressed in terms of milligrams equivalents or International Units of androsterone. The practicability of this test has made possible extensive studies of 17-ketosteroid excretion in normal males and females, as well as in patients with various endocrine disorders. Ostensibly, one primary purpose of these studies has been to determine whether or not a definite 17-ketosteroid value can be associated with a particular pathological condition. If this is found to be true this assay might become an extremely valuable diagnostic procedure.

Androgen and 17-ketosteroid excretion is found in both sexes with the average value for women somewhat lower than those for men. For example, Fraser and co-workers[14] report a range for normal females of 5.1 to 14.2 mg. androsterone per 24 hours with an average of 9 mg. as compared with a range of 8.1 to 22.6 mg. and an average of approximately 14 mg. for normal males.

It is generally assumed that the 17-ketosteroids are derived from the gonads and adrenal cortex. In the male, the steroids are produced by the testes and adrenal cortex.[8,9,14,19] While the studies of Fraser and associates on women with Addison's disease support the hypothesis that all the urinary 17-ketosteroids in the female originate from the adrenal cortex, this remains a controversial point. Callow and coworkers conclude that while 17-ketosteroid values in patients with Addison's disease are generally below normal there is sufficient variation to make the diagnostic value of this test somewhat unreliable.

Large amounts of 17-ketosteroids are excreted by patients with virilizing syndromes due to adrenal cortical hyperplasia or adrenal tumor.[3,5,14,17,22,23,28] The finding of an excessively high value is therefore strong evidence of adrenal cortical pathology. Although the values found in cases of adrenal tumor are generally higher than those in patients with adrenal cortical hyperplasia there is enough overlap to make such determinations unsatisfactory for differential diagnosis. However, the excretion of more than 100 mg. per day has only been found in tumor cases and these very high determinations would therefore be of definite diagnostic value.

In the case of androgen or 17-ketosteroid determinations, as with estrogen assays, it must be remembered that the daily excretion of these substances fluctuate and therefore several determinations should be made before diagnostic significance is attached to the findings.

Pregnandiol Glucuronidate Determinations

In 1937, Venning and Browne[29] recognized that progesterone, secreted by the corpus luteum, is excreted in the form of sodium pregnandiol glucuronidate, a physiologically inactive substance. The chemical structure of this compound was found to be very similar to that of progesterone so that by making correction for the difference in molecular weight, it was not difficult to express the gravimetric determination of pregnandiol glucuronidate in terms of progesterone.

There appears to be considerable individual variation in excretion of this substance ranging from a total of 3 mg. to 50 mg. per menstrual cycle. What this wide variation means is not definitely known but recent studies indicate that progesterone is not quantitatively converted to pregnandiol glucuronidate.[20,30] Since it is present in the urine only during the luteal phase of the cycle, measurements of this substance have been used as a means of determining the duration and functional activity of the corpus luteum. Certain precautions should be taken in evaluating the determinations since zero values have been found in the presence of circulating progesterone. On the other hand, the presence of pregnandiol in the urine may be taken as strong suggestive

evidence of a functional corpus luteum. Its presence is an indication of ovulation, though not a positive one, for it is believed that progesterone can be produced in the absence of ovulation.

In pregnancy, Browne, Henry and Venning[2] report the excretion of 4 to 10 mg. per twenty-four hours up to sixty days. These values approximate those found during the luteal phase of the menstrual cycle. From this time on the rate of excretion rises until near term when the daily excretion may be as much as 80 mg. Occasionally pregnandiol determinations have revealed a drop in excretion at about the time when an increase might be expected. This drop is thought to be due to a lag in the production of progesterone by the placenta. It is of interest that the tendency to abort is most frequently encountered at this time. The theory has been advanced that the uterus is rendered more sensitive and contractile due to a decrease in circulating progesterone. It is on the basis of this theory that progesterone therapy has been used in cases of threatened and habitual abortion. Due to the fact that progesterone therapy is frequently used prophylactically and is usually accompanied by supplemental therapy, it is difficult to evaluate the effectiveness of its use.

There is some evidence that in toxemias of pregnancy of the pre-eclamptic type there is a lowering of pregnandiol excretion.[26,31] The Smiths and their associates[27] have advanced the theory that the lowered progesterone production may be responsible for a change in the metabolism of the estrogens in these conditions. Hain,[16] however, does not subscribe to this therapy since she found large amounts of estrogens and pregnandiol being excreted by a severely eclamptic patient preceding and during labor. Additional information is to be desired concerning the possible association of the pre-eclamptic state with an altered production and metabolism of the hormones.

Conclusions

1. Assays of excreted hormones or related substances may be useful as an aid in the diagnosis of certain endocrine dyscrasias or as a guide to therapy.

2. With the exception of a few tests, such as those for chorionic gonadotropin and pituitary FSH, there are as yet no simple laboratory methods to aid the clinician in the diagnosis of disorders of endocrine origin. Only by thorough investigations can significant data be obtained which may be useful in establishing the nature of an endocrine disturbance.

3. Quantitative determinations of urinary chorionic gonadotropin are useful in detecting the presence of hydatid mole or chorio-epithelioma. These determinations are also of prognostic value in cases of testicular teratoma.

Tests for anterior pituitary FSH are of clinical significance only in instances of marked hypo- or hypergonadism. In these cases the results may give some indication of the therapeutic treatment required.

5. Although estrogen excretion is generally considered a reflection of ovarian activity, variations in rate of excretion limit the usefulness of assays of this substance. The continuous excretion of abnormally large amounts of estrogens is strong evidence of the presence of a granulosa-cell tumor.

6. 17-ketosteroid excretion studies are helpful in determining the cause of virilism since high values are characteristic of adrenal cortical hyperplasia and adrenal tumor.

7. Determinations of pregnandiol glucuronidate may be used as a means of gauging the extent of ovarian function especially with respect to the functional activity of the corpus luteum.

8. It is to be expected that the rapid progress in our understanding of normal and abnormal endocrine physiology will result in greater usefulness of hormone assays.

References

1. Aschheim, S.: Jour. A.M.A., 104:15, 1935.
2. Browne, J. S. L., Henry, J. S., and Venning, E. H.: Jour. Clin. Invest., 26:678, 1937.
3. Callow, R. K.: Proc. Roy. Soc. Med., 31:841, 1938.
4. Callow, N. H., Callow, R. K., and Emmens, C. W.: Biochem. Jour., 32:1312, 1938.
5. Crooke, A. C., and Callow, R. K.: Quart. Jour. Med., 8:233, 1939.
6. D'Amour, F. E.: Am. Jour. Obst. and Gynec., 40:958, 1940.
7. D'Amour, F. E., Funk, D., and Liverman, H.: Am. Jour. Obst. and Gynec., 37:940, 1939.
8. Dorfman, R. I.: Proc. Soc. Exper. Biol. and Med., 45:737, 1940.
9. Emmens, C. W.: Jour. Endocrinology, 1:99, 1939.
10. Evans, H. M., Kohls, C. L., and Wonder, D. H.: Jour. A.M.A., 108:287, 1937.
11. Fels, E.: Zentralbl. f. Gynaek., 53:466, 1929.
12. Fluhman, C. F.: Am. Jour. Obst. and Gynec., 20:1, 1930.
13. Frank, R. T.: Jour. A.M.A., 114:1504, 1940.
14. Fraser, R. W., Forbes, A. P., Albright, F., Sulkowitch, H., and Reifenstein, E. C.: Jour. Clin. Endocrinology, 1:234, 1941.
15. Freed, S. C.: Jour. A.M.A., 117:103, 1941.
16. Hain, A. M.: Jour. Endocrinology, 2:104, 1940.
17. Hamblen, E. C., Cuyler, W. K., and Baptist, M.: Jour. Clin. Endocrinology, 1:763, 1941.
18. Heller, E. J.: Jour. Clin. Endocrinology, 1:813, 1941.
19. Kochakian, C. D.: Endocrinology, 21:60, 1937.
20. Krohn, L., Harris, J., and Hechter, O.: Am. Jour. Obst. and Gynec., 44:213, 1942.
21. Kurzrok, R., Kirkman, I. J., and Creelman, M.: Am. Jour. Obst. and Gynec., 28:319, 1934.

22. Levy-Simpson, S., deFremery, P., and Macbeth, A.: Endocrinology, 20:363, 1936.
23. Patterson, J., McPhee, I. M., and A. W. Greenwood: Brit. M. J., (Jan. 10) 1942.
24. Payne, F. L.: Surg., Gynec. and Obst., 73:86, 1941.
25. Rossler, H.: Ztschr. f. Geburtsch. u. Gynaek., 96:516, 1929.
26. Smith, G. V., and Smith, O. W.: Am. Jour. Obst. and Gynec., 39:405, 1940.
27. Smith, G. V., and Smith, O. W.: Jour. Clin. Endocrinology, 1:470, 1941.
28. Talbot, N. B., Butler, A. M., and Maclachlan, E. A.: New England Jour. Med., 223:369, 1940.
29. Venning, E. H., and Browne, J. S. L.: Endocrinology, 21: 711, 1937.
30. Venning, E. H., and Browne, J. S. L.: Endocrinology, 27: 707, 1940.
31. Weil, P. G.: Science, 87:72, 1938.
32. Wu, H., and Chou, C. Y.: Chin. Jour. Physiol., 11:413, 1937.
33. Zimmerman, W.: Ztschr. f. physiol. Chem., 233:257, 1935.
34. Zondek, B.: Klin. Wchnschr., 9:393, 1930.

MSMS

Hypersensitivity: A Neglected Phase of Allergy*

By Clifford F. Brunk, M.D.
Detroit, Michigan

M.D., Ohio State University, Lt. (jg) U. S. Navy, New York Postgraduate Hospital and Medical School, Chicago, 1920, Teaching at the Chicago Eye and Ear Hospital, Detroit 1921. Hospital Staff Appointments: Harper, Children's Hospital of Michigan, Evangelical Deaconess and Charles Godwin Jennings.

Complement fixation, cultural study, and vaccine therapy, a laboratory aid in diagnosing and treating the hypersensitive patient. Hypersensitiveness is defined as an altered capacity with which cells of the human organism react excessively to contact with particular substances.

Vaccines made from these specific organisms are very potent and must be given in small doses. The dose is kept small throughout the treatment, not to exceed 0.30 c.c., average dose 0.10 c.c.

Better results are obtained from vaccines where primary foci of infection are found and eradicated.

Deficient complement in the patient's blood stream indicates a bad prognosis with any form of treatment, and is a definite contra-indication to surgical interference.

■ HYPERSENSITIVENESS may be defined as an altered capacity with which cells of the human organism react excessively to contact with particular substances. There are other terms in our literature used synonymously or very nearly so. Von Pirquet used the term "Allergy." Coca in 1922 suggested "Atopy." Other authors use the term idiosyncrasy. However, as our knowledge increases concerning this altered capacity of cells to react excessively on contact with certain substances, the term hypersensitiveness is gaining in favor as the one which best expresses this reaction.

Coca, in his book "Asthma and Hay Fever," lists over 1,000 different substances as the cause of hypersensitiveness. Probably though the number of things the human organism may become hypersensitive to is limited only by the number it may come in contact with. The avenue of contact may be through the gastro-intestinal, the upper respiratory tract, the skin, or the sensitizing substance may be elaborated within the system itself.

The cells of the body must dispose of, in some manner, any substance which finds access to the system. Foodstuffs are, through chemical processes, converted into compounds suitable for building or replacing the cell structure, or utilized to produce energy. Other substances, not so utilizable, are changed through chemical processes into compounds easily eliminated.

To many of these substances certain cells of the organism may become hypersensitive, *i.e.*, may take on an altered capacity through which they react excessively on contact with these substances.

The readiness with which a substance may produce a state of hypersensitiveness depends a great deal on the mode of entry. Horse serum for instance, introduced subcutaneously, intramuscularly or intravenously almost universally produces a hypersensitive state. Taken into the gastro-intestinal tract it usually does not.

The substances to which the cell of an organism may become hypersensitive divide themselves into two classes—those which are antigenic and those which are not. A substance is spoken of as antigenic when it is capable of stimulating antibody formation.

Into the class of nonantigenic substances fall those of comparatively simple molecular structure—substances that are readily diffusible through the cell membranes without preliminary breaking down. This class may be illustrated by acetyl salicylic acid, cocaine, novocaine, and quinine.

Antigenic substances are those of more complex molecular structure—molecules too large to be diffusible through the cell membranes, and must be first altered before the cells can dispose of them.

*Read at the seventy-seventh annual meeting of the Michigan State Medical Society, Grand Rapids, September 25, 1942.

The cells, in preparing or breaking down such substances elaborate a chemical commonly spoken of as antibodies. These antibodies then enter into reaction with the substance which we will call antigen with the help of the blood complement splitting them up so that they are diffusible through the cell membranes. These split products produced by the reaction of antigen, antibody and complement are often toxic to the cells and produce the symptoms which we recognize clinically as "Allergy."

Now as to the nature of these toxic substances: The idea that they are lipoids has been advanced, but given very little support.

Gay and Heidelberger have shown rather conclusively that the specific soluble substance, the term they have applied to the toxic product of the pneumococcus, is a complex polysaccharid.

In general, these toxic substances are looked upon as proteins with a carbohydrate radical attached; it is the nature of this carbohydrate radical and its location in the molecule which determines its specificity.

Just what the exact nature of the reaction between complement, antigen, and antibody and the character of the resulting substance is, still is largely a matter of theory due to the complexity of the molecules involved, and the inability to get them in sufficiently pure form for study.

This reaction is looked upon by some researchers as a splitting up of a complex protein molecule into simpler and sometimes highly toxic molecules.

By others it is held that the blood serum contains a ferment and antiferment, which normally neutralize each other, and the antibody complement reaction removes the antiferment leaving the ferment free to break down the more complex molecules into the simpler, more readily diffusible and often toxic molecules. This view is based largely on the recognized toxic properties of some of the peptones and polypeptids when introduced into the blood stream.

Although we are still quite hazy about the exact workings of the reaction between complement antigen and antibody, and the character of new substance or substances formed, we do know and can readily demonstrate that a highly toxic substance may be formed as a result of a reaction involving complement antigen, and its corresponding antibodies. This reaction does not take place in the absence of any one of the three.

It was originally thought that antigen and toxin were separate and distinct substances. But subsequent researches have shown them to be one and the same thing, the difference is in quantity and not quality. In other words—a substance may be present in sufficient quantity to stimulate antibody formation while not sufficiently concentrated to produce a toxic reaction.

Thus far we have considered the sensitizing substances and their reactions with antibody and complement.

To take up for consideration the cells of the organism which react to antigenic substances by the formation of antibody, immediately brings to our attention the so-called reticulo-endothelial system, first described by "Aschoff" some 30 years ago.

The functions of the cells comprising this system are primarily phagocytosis and antibody formation. The main depots for these cells are the spleen, the liver, the bone marrow, the omentum and the lungs. Other cells belonging to this system are scattered in smaller numbers throughout the loose areolar connective tissue of the entire body and are variously described as histiocytes, macrophages, clasmatocytes and resting wandering cells. Under pathological stimulation cells possessing the primary properties of the cells comprising the reticulo-endothelial system may arise from the serous membranes lining the body cavities, the capillary endothelium, the fibroblasts; and also the small lymphocyte of the circulating blood may wander into the tissues, undergo changes and take on the properties of the cells of the reticulo-endothelial system.

Most of these processes we have demonstrated experimentally in the laboratory.

By repeatedly introducing small quantities of antigen into the circulation of a rabbit we can stimulate it to produce circulating antibodies in high concentration.

By introducing a large quantity of an homologous antigen into the circulation of a previously sensitized animal we can completely exhaust the complement in the circulating blood.

The introduction of the same quantity of antigen to which the animal *has not been* previously sensitized alters the quantity of neither antibody nor the complement.

If the cells of the reticulo-endothelial system

are first blocked by the introduction of an adequate amount of colloidal carbon in the form of india ink we are unable to stimulate any appreciable amount of antibody formation.

When an animal so treated is sacrificed and the tissues sectioned we find the cells of the reticulo-endothelial system clogged with phagocytosed carbon particles.

If an animal is first sensitized and then india ink injected we find on sacrificing it that the main depots of reticulo-endothelial cells much more heavily loaded with carbon particles. This is due to hyperplasia of these cells in the sensitized animal.

By sensitizing the skin of a rabbit with repeated intracutaneous injections of an antigen we can demonstrate the formation of these cells from the fibroblasts; also lymphocytes may be seen undergoing similar changes. When the sensitizing antigen is a suspension of bacteria we can demonstrate phagocytosis of the bacteria.

It is this sensitizing bacterial toxin or antigen liberated by a focus of infection which we are endeavoring to evaluate in this study. If we accept the hypothesis of bacterial sensitization our problem then is to determine the source of the offending organism, also its virulence, that is, its capacity to produce sensitizing toxins. We must also determine the reaction of tissue cells to these toxins.

It is well established that hypersensitive tissues form antibodies in excess, the cells become over-saturated with antibodies, and the excess is released into the circulation.

In our laboratory we have developed a form of complement fixation for detection of the complement fixing antibodies, by a modification of this test, we are able to determine the antigen producing properties of organisms recovered from foci of infection. We are using this test because it is considered the most sensitive and the most economical, when using a large number of antigens. At present we are using about 35 antigens, which include colon bacillus, micrococcus catarrhalis, staphylococcus albus, and aureus, and the different strains of streptococcus—hemolytic, nonhemolytic and viridans. The complement fixation test of the patient's blood against these antigens shows which organisms are stimulating excess antibody formation, that is, the specific organism to which the patient is hypersensitive.

We then culture all accessible tissues of the patient including urine and bowel contents. The cultures are collected in a media of beef heart infusion broth, then transferred to blood plates within two hours. There it is allowed to grow from 12 to 48 hours. Then individual colonies are picked up and put into brain broth and incubated 24 hours. It is then checked under a microscope to be sure it is a pure culture. If there is no contamination it is again placed into 10 c.c. of beef heart infusion broth for growth of organisms in sufficient quantity to make an autogenous vaccine, and for tests of antigen or toxin producing qualities. Cultures are also planted on sugars for differentiation of the individual strain of organism.

The patient suffering from bacterial hypersensitiveness complains of a chronic pharyngitis, and congestion of the nose usually present the year round, more marked during the changing seasons. Other constitutional symptoms may be the various forms of rheumatism, arthritis, myositis, neuralgia, and iritis. We also believe that some forms of asthma and urticaria, and states of debility not otherwise explained, may be included in this group.

Once we have determined the offending organisms and have located the focus of infection, the treatment is primarily surgical; by this we mean the actual removal of the pathological tissue, and the surgery must be adequate, not necessarily radical, yet complete enough to remove the focus.

However, our blood and cultural studies will have a decided influence in the treatment of any given case. We do as little surgical interference as possible in the acute phase of the infection. This is the stage when the toxins are being produced more rapidly than antibody formation.

Another important factor disclosed by the complement fixation test is the amount of complement present in the blood. We don't know exactly what this substance is. We do know that it is present in all normal blood in sufficient quantity to unite antigen or toxin with the antibody produced by the reticulo-endothelial structures.

Occasionally, we find a patient seriously lacking in complement. This is a danger signal as no toxin will be fixed by antibodies. This may be the explanation of our deaths in cases of mild infections, or following minor surgical procedures. These cases are subjected to no surgical

interferences until the presence of complement has been confirmed by another Complement Fixation test.

This treatment will cover a large number of your cases. However, when the focus, if found to be located beyond the reach of surgery, such as in the intestinal tract or prostate gland, or when the patient is not a good surgical risk, due to insufficient complement, bad temperament, age or physical condition, and, as is often the case, his immunity is so broken down that even after the foci have been removed, he will not respond to dietary or medical care, then we make an autogenous vaccine and attempt to desensitize him by a course of vaccine treatments.

The vaccine consists of the antigen producing organisms recovered from the patient, and those organisms to which the patient is sensitive as shown by the complement fixation test. The organisms are subcultured only twice, and no stock or laboratory grown organism used. Each vaccine may have from five to twelve strains of organisms.

The vaccine is made up in a dilution of from 50 to 200 organisms of each strain per cubic centimeter. The dose is regulated by the reaction of the patient. When the patient presents acute symptoms, such as an inflamed joint or acute iritis, they are very likely to have a marked reaction to even a small dose.

When no acute symptoms are present they will usually tolerate a larger dose without reaction. However, we have seen marked reactions in just such cases, even with a small dose. We try to regulate the dose so that the patient gets no reaction. To arrive at this it is usually necessary to carefully increase the dose to the point of slight reaction, then decrease again. If we get no reaction with a reasonably large dose, say 5 c.c., we do not believe that the vaccine is of much value.

The initial dose is 0.1 c.c., the subsequent doses increased or decreased according to reaction. In obtaining our best results we have seldom given more than 0.3 c.c., nor less than 0.02 c.c.

The interval between inoculations is judged by the patient's feeling of well-being or response to the vaccine. There is usually an improvement after each injection, lasting from four to five days, then a recurrence of symptoms, so we make our interval five days. This gives definite, though sometimes slow improvement in the general situation. In unfavorable reactions the patient has an increase of symptoms and fatigue. We have had no local inflammatory reaction nor anaphylactic shock in our experience. Apparently the important thing is proper regulation of dosage. In a viable vaccine the dose is small.

We now have a great respect for a properly prepared autogenous vaccine. Its action is specific, and if not properly controlled, may do more harm than good.

Our findings are based on the study of 5,000 private patients. The laboratory findings have been a distinct help in diagnosing and treating the hypersensitive patient.

Summary

1. Complement fixation, cultural study, and vaccine therapy, a laboratory aid in diagnosing and treating the hypersensitive patient.

2. Vaccines made from these specific organisms are very potent and must be given in small doses.

3. Better results are obtained from vaccines where primary foci of infection are found and eradicated.

4. Deficient complement in the patient's blood stream indicates a bad prognosis with any form of treatment, and is a definite contra-indication to surgical interference.

MSMS

POLIOMYELITIS CONSULTATIONS

The Michigan Crippled Children's Commission has sent to every County Medical Society Secretary, and to every full-time Health Officer, a Bulletin announcing that the Commission again this year establish poliomyelitis consultation service as it has in the past, for children up to twenty years of age. This is the original consultation by which the diagnosis is established.

The details of procedure are on file with the secretary of the County Medical Society and the full-time Health Officers, who should be contacted when such consultation is needed. The State is divided into fifteen districts, and both pediatric and orthopedic consultants available are listed.

It should be thoroughly understood that this service is only for those cases where the families are unable to make their own arrangements.

Intracapsular Cataract Extraction

With a Modification of Dimitry's Suction Syringe*

By J. Conrad Gemeroy, M.D.
Detroit, Michigan

M.D., 1926, McGill University, Certificate American Board of Ophthalmology and American Board of Otolaryngology, Fellow American Academy of Ophthalmology and Otolaryngology, F.A.C.S.

■ CATARACT extraction with a suction is not new but since Dimitry's experience with his improved suction syringe, a great many things have been said for and against the use of such an apparatus for removing cataracts.

It was because of such comments that we purchased a Dimitry syringe and decided to try it. This is an endeavor to report the results in fifty cases in which a modification of Dimitry's Suction apparatus was used in performing intracapsular cataract operations.

In addition six other cases are included in which Dimitry's modified syringe was used to deliver the lens after other methods had failed.

In the first few cases Dimitry syringe only was used (Fig. 1). However, it was soon found to be difficult to use the syringe between two fingers and with the thumb on the plunger. The tendency was to transfer the grasp of the syringe down on the barrel near the suction tip between the thumb and first two fingers in an endeavor to handle the syringe (Fig. 2). It seemed logical that if the syringe could be held that way at all times and after introducing it into the anterior chamber, be able to let the plunger come up and produce the suction, the whole thing would be simplified, and this instrument would be handled with the thumb and first two fingers like any other eye instrument, such as an iris forceps. With this in mind such a modification was made of the Dimitry apparatus which simplified the delivery of the lens after the suction had been applied (Fig. 3).

With this modification, one is able to hold the syringe at all times between the first two fingers and thumb, while introducing it into the anterior chamber while releasing the plunger, creating the suction, and then on throughout the delivery of the lens and the capsule.

All cataract patients received a drop of 1 per cent atropine the night before operation and another the next morning to dilate the pupil as widely as possible. Anesthesia consisted of local 0.5 per cent of pontocaine to the cornea and conjunctiva, one drop every three minutes for six drops. In addition 4 per cent novocaine was used for the following: 1.5 c.c. injected into the muscle cone to anesthetize the ciliary ganglion, 1 c.c. of 4 per cent novocaine in the upper culdesac to facilitate inserting a superior rectus suture, and just enough in the lid margins to place sutures for retraction. Sutures were substituted for mechanical lid retractors because they caused less pressure and took less space. A Van Lint akinesis of the lid is also done with 2 per cent novocaine.

A bridle suture was used in all cases and the lids were held open by means of sutures through the skin margins, two above which were anchored and one below which was held by the assistant.

Section was made with a Von Graefe knife ending with a small conjunctival flap. Conjunctival sutures were inserted and pulled out of the way before proceeding.

Iridectomy was done on all cases in which the pupil was not sufficiently dilated. This was done in about two-thirds of the cases. Otherwise the lens was removed through a round pupil or after a basal iridotomy.

The suction tip was passed into the anterior chamber and was allowed to grasp the lens as near the top of the lens as the iris or iris pillars will permit, after an iridectomy. With a spoon or muscle hook the zonular fibres were broken below as in any other intracapsular operation. Then with pressure below (at 6:00 o'clock) the syringe was slowly elevated through about twenty-five degrees. This combined with the pressure below lifted the lens up into the anterior chamber and it was then slowly pulled and expressed out of the eye. The conjunctival sutures were tied and if the iris were protruding, it was replaced in the eye. Before padding the eye two drops of 1 per cent esserin was instilled in the eye.

Some surgeons place the suction tip at or near 6:00 o'clock. This necessitates tumbling the lens. The method described above does not tumble the lens but simply helps bring it up into the anterior chamber and then out of the eye.

*Read at the seventy-seventh annual meeting of the Michigan State Medical Society, Grand Rapids, September 25, 1942.

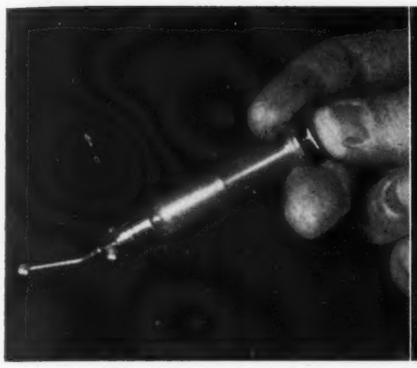


Fig. 1. Dimitry suction syringe held between two fingers with thumb on plunger.

Fig. 2. Dimitry suction syringe held near the base in an endeavor to control it better.

Fig. 3. Dimitry suction syringe with modification which allows one to hold the syringe between the thumb and second finger, the index finger being able to release the suction when desired.

In this series of fifty cases an iridectomy was performed in thirty-five cases and in the remaining fifteen the lens was delivered through a round pupil. The reason for not doing an iridectomy in these fifteen cases was due to extreme dilatation of the pupil. A significant fact is that postoperative complication of prolapsed iris occurred in two round pupils.

Types of Cataracts

(Impressions made with the slit-lamp before surgery was done.)

Hypermature	4
Mature, complicated with diabetes	5
Congenital, with congenital coloboma, and extremely small eye	1
Immature with visual acuity of 20/200 or less. (Judged immature because of a dark band between capsule and lens nucleus)	12
Mature with no soft lens substance between nucleus and capsule	16
Mature but nucleus of the brown hard morgagnian type, those that are hard to tumble or mold during the operation	12

In reporting these results, it should be emphasized that though fifty cases are not sufficient to make any mature judgment, the results are interesting especially in a discussion of the failures. Therefore, no attempt will be made to be purely statistical.

All told, Dimitry's modified suction was used in fifty-six cases. In fifty of these the instrument was used alone and in the other six the instrument was used to deliver the lens after some other type of intracapsular surgery had already been tried and failed. A discussion of these six cases is also of interest.

Average age was fifty-nine years, all were over forty-five years except one case and that was a seventeen-year-old congenital diabetic. One reason for trying to deliver the lens in this case was based on previous disastrous experiences in needling such cases. This was one of the failures, simply because the zonular fibres were too strong. This case proved definitely just how much suction the apparatus gave before it came off. It did not rupture the capsule though replaced twice after coming off as a result of too much pull. In this case after failing to deliver the lens by suction the anterior capsule was opened and the soft lens substance washed out. The final visual acuity was most gratifying for a diabetic of this age.

Of the fifty cases forty-three were successful (i.e., the lens was removed in its capsule). Seven cases were unsuccessful. Four of these capsules ruptured before the lens could be delivered necessitating capsulotomy and expression of the lens nucleus. All four of these were in hypermature cataracts, which is significant. This type is the most difficult to remove in its capsule using the forceps and tumbling method.

The fifth was the seventeen-year-old congenital diabetic previously referred to. In another case the suction would not hold. Whether part of the iris was in the suction tip or whether the apparatus was not working is not certain. It was the only instance in which the suction would not take hold.

The seventh failure was in a very shallow anterior chamber, and perhaps the section was not large enough. In introducing the suction, the tip ruptured the capsule of the lens before suction could be applied.

These last two were finished with a capsulot-

omy and expression of the lens nucleus as in an ordinary operation.

The six cases in which the suction syringe was used to deliver the lens after other methods of delivery had failed are worth comment. In five of these forceps were used and the lens partially tumbled when the forceps came off and let the lens either fall back into its original place or in on case turned half over. Rather than use a loop, the suction was used to grasp the lens and hold it so that it could be expressed out of the eye. These cases alone justified the purchase price of the apparatus.

The sixth case is worth summarizing in greater detail. This was a congenital small eye with congenital coloboma and blind in the opposite eye. The operation of choice was naturally a capsulotomy and expression of the lens through the enlarged coloboma. Everything went fine; an extremely large section was made to begin with, but the lens could not be expressed no matter how much manipulation. As a last resort the suction was applied to the lens itself even after capsulotomy and was successfully delivered.

These six cases might be considered complicated cases, but they were included because we felt the use of the suction syringe had helped to get us out of a difficult situation.

Of the complications some of them are interesting, namely loss of vitreous, prolapsed iris, secondary glaucoma and detachment of the retina.

Vitreous was lost in seven cases, in three cases of the forty-three successful operations, in two of the seven unsuccessful cases and in two of the complicated series of six where the suction had been used as an aid after other methods had created a difficult situation.

In the successful series vitreous was lost just at the end of the operation in two cases, and it was probably due to too much push from below. In the third case it followed the replacement of a prolapsed pillar and was not due to the suction syringe at all but to rupture of the vitreous membrane by the iris repository.

Of the two cases in the seven unsuccessful series trauma from too much manipulation could only explain the rupture of the vitreous membrane which followed the lens expression.

In the two cases in the complicated series it was undoubtedly due to the same cause and came at the end of the operations, but considering everything it was a very easy payment in a difficult situation.

A significant fact worth noticing is that no loss of vitreous occurred in all cases whether in the complicated series of six or the original series of fifty as a direct result of vitreous being sucked into the syringe. This fact is significant.

Other complications were from the operation and not due in any way to the use of the suction syringe—

First, prolapsed iris occurred in two cases which needs no comment; again secondary glaucoma in two cases and both of these were rather difficult to handle and accounted for two of the poor postoperative vision in the series.

Another complication was three cases of detachment of the retina in the fifty-six cases, two of which ended rather disastrously as regards visual acuity and the third after operation for detachment has now a visual acuity of 20/70. One patient lost his eye completely and that due to a massive choroidal hemorrhage. The operation was successful and he left the operating room with an excellent eye but three hours later he complained of pain in the operated eye. Shortly after the dressing became soaked with blood and a second dressing as well. Observation of the eye showed the wound open and a large blood clot in the wound filling the anterior chamber. The eye was eventually removed and section of it showed the eyeball to be filled with blood clot.

Comment

It is not possible to make any mature comments with only fifty cases. A much greater series would be necessary.

The following are listed and might be considered impressions made rather than mature deductions:

1. Extraction by means of suction is one way of doing an intracapsular cataract operation but by no means the only way. It is simply another method to add to the many other equally successful methods.

2. With continued use one may become quite adept in delivering a lens in its capsule with a suction. Most of the failures occurred early in the series and might be considered as due to trying a new method.

3. It is not the only method to be used in all types of cataract removal. Its failure especially in the hypermature cataract in this series was par-

ticularly noted. This type of cataract has always been most difficult to remove in its capsule with the forceps and tumbling method.

4. It is a less delicate way than the use of forceps. One has to be more dexterous to deliver a lens in its capsule with forceps and tumbling it out of the eye.

5. The suction syringe of Dimitry is worth having in one's bag of instruments as another help which is illustrated in its use in the six so-called complicated cases.

6. An interesting observation is that the senior member of our staff who has been doing intracapsular surgery with forceps for years, after trying Dimitry's suction a number of times finally reverted back to the use of forceps feeling he could do his best work that way.

This last statement sums up all comments on the pros and cons of cataract surgery. It is not the way one does it but the end result that always counts.

MSMS

Vaccine Therapy in the Treatment of Uveitis*

By Henry A. Dunlap, M.D.
Detroit, Michigan

M.D., University of Michigan, 1929, Certificate American Board of Ophthalmology, Fellow American Academy Ophthalmology and Otolaryngology.

■ THIS discussion intends to review the various forms of vaccine administration as an adjunct to other treatment for acute, recurrent and chronic forms of uveitis. In addition, it will accent a particular method for developing a specific vaccine used in desensitizing by repeated small subcutaneous doses, patients with endogenous uveitis, frequently referred to as having an etiologic background of focal infection, or primary foci.

Foreign Proteins

Newton in 1935 published a report on accepted uses of vaccine in his "Empirical Treatment of Uveitis," mentioning in this paper, particular preferences of various clinicians. Of the foreign proteins, typhoid vaccine was given by the majority, in initial doses of 25,000,000 intravenously, following on recovery from the resulting fever with a second dose, increasing or decreasing in size dependent upon the first reaction. Thereafter, subsequent doses are repeated on alternate days. This is a useful treatment in most forms of uveitis, regardless of etiology, even though the precise nature of beneficial reaction from foreign protein is little understood. It is not recommended in malignant exudative forms of tuberculous uveitis, or in individuals where advanced age or other contraindications exist. For those not able to risk typhoid vaccine, a more moderate substitute can be utilized, such as Typhoid "H" antigen, this also being useful in chronic forms where long continued usage is desired. Milk, diphtheria antitoxin, and bacterial antigen have been given, the latter recommended by Weiner. Milk is widely used with a dosage of 5 to 10 c.c. intramuscularly. With diphtheria antitoxin, one must be particularly careful of serum reactions and first test for sensitivity. Würdemann has used rheumatism bacterial filtrate of pathogenic organisms.

Killed broth culture of prodigiosus and streptococcus fluid has been given by Joseph Levine in 3 minim doses intravenously, the patient having four to five hours in which to get home before suffering the reaction, this lasting twelve to twenty-four hours.

Typhoid vaccine offers us a foreign protein with powerful reaction and this is preferred where milder reactions will not give the desired clinical response.

Foreign protein may be of value in tuberculous forms of uveitis in addition to tuberculin therapy. It may enhance the beneficial effect from antiluetic therapy in syphilitic uveitis.

Patients with recurrent uveitis or acute exacerbations of the chronic type will sometimes present themselves voluntarily for periodic injections of mild foreign protein when a flareup is imminent, with beneficial results.

The tuberculin treatment of the tuberculous uveitis was described well by Adler and Meyer in 1937 in their paper on "Tuberculous Lesions of the Uveal Tract" with a review of the literature. It is a method of dosage with which most authorities are in agreement, and it is generally accepted that the aim is desensitization with doses kept below the point of local and focal reaction, necessarily used over a long period of time.

*Read at the seventy-seventh annual meeting of the Michigan State Medical Society, Grand Rapids, September 25, 1942.

Etiology

I have not adhered strictly to the title of this paper according to Woods definition of vaccine therapy, this therapy being essentially active immunization of the patient with specific organisms. Alan Woods brought to date in 1933 the work done in vaccine therapy in his monograph "Allergy and Immunity in Ophthalmology." A consideration first as to the etiologic importance of focal infection is advisable. Grayton and Woods in 1941 analyzed 562 completely studied hospitalized cases of uveitis and gave a comprehensive report of the etiology of uveitis. Their percentage of cases with definite evidence of etiologic factor credited 23.5 per cent to tuberculosis and 8.0 per cent to syphilis as compared to 5.5 per cent to foci of infection. For the patients with presumptive evidence the percentage attributed to tuberculosis was 26.1 per cent making a total of 49.7 per cent, that for syphilis was 2.5 per cent, making a total of 10.5 per cent, and for focal infection 20.6 per cent or a total of 26.1 per cent. The authors particularly emphasize the large number of cases presumed due to focal infection as being on shaky ground, and state that there is an element of doubt as to the accuracy of any diagnosis in which uveitis is attributed to a focus of infection. This is a statement difficult not to accept, proof to the contrary seeming so evasive.

Yet when one selects a group of patients, for any reason, out of a much larger group of patients having a diagnosis of uveitis one immediately introduces a misleading element in the statistics. The fact that 562 patients were hospitalized probably places them in a group by themselves, a total of 1500 cases having gone through the clinic. Duke Elder in his Textbook of Ophthalmology, Vol. III, throws the majority of uveitis cases into a nondescript, little understood classification with etiology difficult to prove. He believes allergic reaction to the streptococcus as the most common cause of endogenous uveitis, placing allergy to the tubercle bacillus second. He of course admits the difficulty of proof and the necessity to base conclusions on circumstantial evidence.

Allergy

If there is a group of uveitis due to an allergic ocular response to the staphyloccus and streptococcus in activated primary foci of infection, and if there is a method for supporting other treatment by desensitization to the offending organisms so that natural immunity may protect the ocular structure from further damage, it would be of considerable interest. Woods, in 1940, stated:

> "When the complexity of bacterial hypersensitivity and vaccine therapy are considered, there appears to be little justification for many of the present therapeutic procedures with bacterial vaccines and products. It must be conceded that in the majority of instances it is only shotgun therapy and any beneficial results observed are quite as likely to be general nonspecific effects as to be the specific reactions to the injected bacteria."

Applebaum, in 1940, discussed bacterial allergy in the eye associated with foci of infection and his conclusions are based on experimental evidence of many investigators. An immunity is acquired by the formation of circulating antibodies on exposure to an antigen and this will protect to a degree against later exposures to the same antigen. Tissue cells may become sensitized by fixed antibodies producing a degree of hypersensitivity or state of allergy. The balance of the immunity and hypersensitivity will determine the severity or mildness of a reaction in the individual, either general or local. Immunity can thereby temper the reaction to doses of antigen, depending upon the degree of cell sensitivity. This is well demonstrated in tuberculosis.

Focal Infections

Experimental work points to the conclusion that bacterial infection can produce definite hypersensitivity in the ocular tissues. The bacterial products or toxins may reach the eye from a remote focus through the blood or lymph, and subsequent absorption of bacterial products or toxins from a primary focus evokes in the sensitized tissue an allergic inflammatory reaction. Swift and Derrick definitely showed that the ideal manner of creating allergic states was by chronic absorption from a limited focus, where tissue destruction occurred. Clinical proof is difficult to bring, as experimentation with the human eye is usually impossible, and as Woods expresses it, the best evidence that can be produced will probably be proper desensitization of such patients accompanied by clinical improvement in the eyes.

Circumstantial evidence of the relationships between foci of infection and uveitis is in abundance. To mention a few examples met with personally:

Extraction of teeth in the presence of active pyorrhea followed quickly by focal reaction and rapid quieting of the inflamed eye. Focal reaction in the same patient from a small subcutaneous injection of specific vaccine, some organisms of which were recovered from the pyorrhea pockets.

Many examples of focal reaction in the eye following massage of a chronically infected prostate, or the case of acute flareup of uveitis, repeatedly following horse back riding in the presence of an active anal cryptitis.

Active nasal and sinus inflammation yearly on return from Florida to Michigan, always followed by recurrent attacks of uveitis, and this only active at such a time.

To offer more specific proof and properly desensitize, one must know not only the organisms responsible, but all of their characteristics so that a vaccine can be made up as nearly specific as is possible. Thus, a stock vaccine is no more than shotgun procedure.

Skin testing is difficult to evaluate since a high percentage of normal adults will react in a positive manner to the streptococcus or its by-products. Berens cultured organisms obtained from foci and interpreted their specificity by skin testing the patients, but no good conclusions were drawn, although 14 of 17 given therapy improved.

Specific Vaccines

S. W. Wallace of Jennings Hospital, Detroit, has been interested for years, both experimentally and clinically, in producing a specific vaccine obtained by evaluation of the complement fixation studied to many pathogenic bacteria, and careful and complete culture studies of organisms obtained from all possible foci. In a discussion of bacterial hypersensitivity given at this same meeting, this method of study is more particularly analyzed and described by C. F. Brunk.

In attempting to correlate this work with uveitis, I have had too few cases for statistical analysis, but the experience points to future possibilities of more close clinical study of this group of patients. With careful cultural studies made to determine the characteristics and antigenic strength of organisms obtained from foci, and the knowledge of abnormal hypersensitivity to definitely known strains of bacteria, one is, I believe, in better position to evaluate the importance of a focus.

In study of the patient, a complete medical examination is necessity, with laboratory and x-ray aids to rule out other possible etiologic factors.

Cultures are taken routinely, of the nose and throat and stool, with additional studies made where indicated or possible, of pyorrhea pockets, extracted teeth, anal crypts, prostatic secretions, urine, cervix or of surgically removed infected tissue. These are carefully studied for classification on sugars and the antigenic properties of each organism determined by running against 4 to 6 known sera of certain complement fixation reaction. Each strain is tested in this manner.

A blood sample of the patient is taken during this time, and studied for complement fixation reactions following the technique developed by Hajapoules and Burbank of New York. Bordet and Gengou, in 1901 clearly described the phenomena of complement fixation. They described a third substance necessary to effect union between an antigen and its specific or corresponding antibody, and this was termed complement or alexion. Complement is a more or less constant element of blood serum which is closely associated with the globulin fraction of the serum protein from which it has never been successfully separated. It is nonspecific and unites with any antigen antibody combination.

Technique

The technique by Wallace utilizes 35 separate pathogenic antigens selected for activity and toxin producing qualities or properties. These are run separately with measured quantities of the patient's serum, to determine whether the antibodies are present for these specific antigens to unite with, and in what degree. The fixation and its degree is measured by the amount of complement left free. Experimental work with rabbits proved the reliability of specific antibody formation, results being consistent.

The antigens are standardized so that comparisons may be made with the average normal individual for interpretation.

Three types of variations are found in the test:

1. Diminished or depleted antibody.
2. Excessive antibody.
3. Diminution or exhaustion of complement.

With the culture and complement fixation studies at hand attention can be turned to the focus which shows the presence of toxin-producing organisms with strong antigenic properties. This

would deserve eradication or treatment if possible, whereas a suspected focus without organisms of this type may be considered innocent. It is in the first situation that best results are obtained by removal of foci.

Vaccine can be prepared by utilizing the important organisms found on culture, and adding to this any of the strains of antigens to which the blood serum of the individual proved excessive antibody formation, since this type of reaction is that found in the allergic or hypersensitive state. This vaccine will then be more than an autogenous vaccine, having a number of the commoner antigens to which the patient is sensitive. It is therefore considered specific, although with all this study, there are still limitations as to obtaining all offending antigens or complex proteins.

If a definitely toxic focus is removed, time is given for recovery of the secondary allergic inflammation and if not successful, vaccine is used in desensitizing doses, using minute doses of dilute vaccine and keeping the dosage small. Vaccine is also used where there is no definite indication for removal of foci. It is given every five days for at least three months. One will expect to get gradual improvement in chronic forms of uveitis and a disappearance of recurrences or diminishing severity of acute attacks if the vaccine is of any help.

In uveitis as well as in several cases of allergic type of kerato-conjunctivitis, there have been focal reactions with small doses of this vaccine, indicating specificity, and necessitating further dilutions until sufficiently desensitized.

Most of the cases studied in this manner where other causes have been ruled out have shown improvement where a well-established focus has been removed or treated. A few in addition have derived benefit by following this with the vaccine therapy. The eyes have remained quiet or the recurrences have decreased in frequency and severity. Thus, this approach to the problem may be of benefit more because of a thorough evaluation of the importance of foci, rather than the vaccine developed. However, the vaccine has possibilities as supplemental therapy and may some day be better understood.

MSMS

You owe much of your medical security today to the past activities of organized medicine. You have an obligation to those who follow. Will you help carry on?

The Significance and Management of Joint Pain*

By Charley J. Smyth, M.D.
Eloise, Michigan

and

Richard H. Freyberg, M.D.
Ann Arbor, Michigan

CHARLEY J. SMYTH, M.D.
M.D., 1935, Jefferson Medical College; 1935-38 Intern and Assistant Resident Depts. of Medicine and Pathology, University Hospital, Ann Arbor; 1938-41, Instructor Dept. of Medicine and Research Assistant in Rackham Arthritis Research Unit, University of Michigan; 1941, Medical Director William J. Seymour Hospital, Eloise, Michigan, and Instructor in Medicine, Wayne University, Detroit.

RICHARD H. FREYBERG
M.D., University of Michigan, 1930; Research Director of the Rackham Arthritis Research Unit, University Hospital, Ann Arbor. A Fellow of the American Medical Association; Associate, American College of Physicians; member, American Rheumatism Association, American Society for Clinical Investigation and the Central Society for Clinical Research.

Pain is an important factor in incapacitating patients with acute joint disease and in the production of deformities in chronic joint disease. The joint tissues receive their nerve supply from mixed nerves and terminate as free nerve endings in a nerve plexus or in special nerve organs. The importance of pain in the differential diagnosis of joint diseases is emphasized. In the treatment of arthritis and allied disorders satisfactory analgesia can usually be accomplished by the proper use of rest, splints, drugs, roentgen irradiation therapy and other physical measures.

■ PAIN is usually the one symptom which compels a patient with joint disease to seek the aid of a physician. In such a case unless the cause for the pain is immediately evident, many physicians are inclined to attribute the symptoms to rheumatism or neuritis, and to advise symptomatic treatment. The results of this program of management are frequently unsatisfactory and have led some doctors to assume an attitude of

*From the Rackham Arthritis Research Unit of the Horace H. Rackham School of Graduate Studies and the Department of Internal Medicine, the Medical School, University of Michigan. Read at the seventy-seventh annual meeting of the Michigan State Medical Society, Grand Rapids, September 25, 1942.

defeatism regarding the treatment of painful joints. This attitude certainly is not justified, because if a specific diagnosis is made, satisfactory treatment can be instituted. It is the responsibility of each physician in every community to recognize and adequately treat patients with arthritis and allied painful joint conditions, otherwise they may fall prey to quacks and charlatans.

We have been impressed that pain and its control is one of the major concerns of the physician confronted with a patient suffering from arthritis. A careful search of the literature, however, revealed a striking lack of information regarding the factors responsible for joint pain and of the pathways over which painful impulses from joints reach the higher centers. The present discourse is a result of an investigative study of the present knowledge of joint pain and an interpretation of this information as it applies to the diagnosis and management of patients who complain of joint discomfort. It is further intended to indicate the necessity of a comprehensive knowledge of this important symptom for the establishment of rational methods of therapy in some of the more common joint diseases.

Innervation of Joints

As a basis for an understanding of joint pain we studied the distribution, type, number and function of nerves in each tissue composing a joint. The complete results of this study will be the subject of another publication. For the purpose of this discussion it is sufficient to know that the joints receive their nerve supply from the mixed nerves which also innervate the muscles, bones and skin of that area. The articular branches enter and richly supply the joint capsule and distribute terminal branches of unmyelinated and finely myelinated fibers to the ligaments, periosteum and synovial membrane. We found no nerve fibers in the cortical bone or in the articular cartilage. The nerves terminate in one of three ways: as free nerve endings, in a nerve network or plexus, or in special nerve organs.

Physiology of Joint Pain

There are some accepted principles regarding the physiology of pain that apply to the interpretation of this sensation in joints. It has been shown by Adrian[1] and confirmed by Heinbecker and Bishop[5] that impulses produced by painful stimuli are distinct from those produced by pressure or touch and that pain impulses are conducted only over pain fibers. This principle is now generally accepted and we can conclude that painful sensations from joints are carried along fibers which transmit no other sensations.

Recent evidence presented by Gasser[3] and confirmed by others indicates that the sensation of pain is mediated by fine unmyelinated or finely myelinated nerve fibers. The free nerve endings and the terminal nerve plexus in joint structures are morphologically like the fibers described by Gasser and it seems logical to allocate to them the specific function of pain reception.

There are a few references in the literature regarding the question of the mechanism which serves to initiate pain in joints. The factors in joint disease most likely responsible for pain are the stretching of the terminal plexus or nerve net by hyperemia, edema and inflammatory exudate. Another contributory factor is the stretching and traction caused by muscle spasm on the sensitive endings in the periosteum at the site of the tendenous insertions. Improper balance adds to the traction and strain on both the ligaments and the joint capsule. In the late stages of joint disease erosion and irregular jagged surfaces exert pressure on nerves which normally were protected.

It has long been recognized that protective muscle reflexes are always associated with pain. For example, if a nerve to an extremity is stimulated, the flexor muscles contract and the extensor muscles relax. This response is due to the reflex inhibition of the opposing muscle group and is one of the mechanisms responsible for flexion contracture deformities in chronic joint disease. At the knee, for example, chronic inflammation may set up continuous pain stimuli which result in continuous spasm of the flexor muscles and a reflex relaxation of the extensor group, so that if continued long enough flexion contraction may result. The importance of breaking this reflex arc by keeping the patient as free of pain as is possible at all times cannot be overemphasized.

Referred pain in joint disease is worthy of some attention because certain joints give rise to pain in skeletal parts removed from the affected joints and this may lead to improper therapy. Lumbo-sacral and sacro-iliac pathology is commonly accompanied with pain referred to the gluteal region, posterior thigh, posterolateral

calf and lateral border of the foot. The pain of hip joint disease is characteristically felt in the anterior groin, down the inner part of the thigh or in the mesial aspect of the knees. At times hip joint lesions will be overlooked because the patient complains of pain only at the inside of the knee or just beneath the patella.

The recent finding of small inflammatory nodules along the course of peripheral nerves in patients with rheumatoid arthritis by Freund, Price, Steiner and Leichtentritt[2] offers an additional basis for pain, paresthesias and trophic disturbances in these patients. These multiple perineuritic lesions probably act by causing irritation of the sensory nerve fibers.

One of us (C.S.) has studied the relationship of joint pains to various weather changes in twenty arthritic patients. Several of this group claimed the traditional ability to predict weather changes by the increased joint discomfort preceding a rain or a storm, but close observation revealed their predictions to be wholly unreliable. There was no constant relationship between the changes in joint pain and changes in climatic temperature, relative humidity or barometric pressure.

Clinical Problems

From a practical clinical standpoint the management of joint pain can best be accomplished after a specific diagnosis is established. Because of the great variety of conditions having joint symptoms at one time in the course of the disease a careful study may be necessary to determine the exact etiology. The accompanying table, which is by no means complete, will serve to emphasize this point.

For an accurate diagnosis it is often of considerable value to obtain a complete description of the pain, including: (1) its localization, (2) the character, (3) whether constant or intermittent, and (4) factors causing exacerbation or relief. By the intelligent interpretation of this information the diagnosis, probable location and character of the lesion may be determined.

The conditions which will be discussed here represent those most commonly met with and for which we have at our disposal satisfactory methods of therapy. It is well to remember that in the management of joint disease the control of pain, although an important part of treatment, is only the control of one symptom and other local and general symptoms should receive equal attention.

TABLE I. EXAMPLES OF THE DIVERSE NATURE OF DISEASES FREQUENTLY PRESENTING JOINT SYMPTOMS

1. *Common forms of arthritis*
   rheumatoid arthritis
   hypertrophic arthritis
   rheumatic fever
2. *Non-articular rheumatism*
   fibrositis
   periarthritis
   bursitis
   tenosynovitis
3. *Generalized infection*
   meningococcic arthritis
   gonococcic arthritis
   pneumococcic arthritis
   tuberculous arthritis
   brucellosis arthritis
4. *Neuropathic arthritis*
   tabes dorsalis
   syringomyelia
5. *Metabolic arthritis*
   gout
   menopausal
6. *Miscellaneous forms*
   hemophilia
   intermittent hydrathrosis
   scleroderma
   traumatic
   neoplastic
   serum sickness
   ulcerative colitis
   psoriasis

Cervical Pain.—The painful stiff neck is frequently a puzzling diagnostic problem which is far too commonly referred to as a "neuritis." The majority of cases of so-called cervical neuritis are due to joint disease and not primarily to any neurological condition. Irritation of nerve roots as they emerge from the spinal canal is frequently produced by impingement of a bony spur or by fibrotic tissue associated with spinal arthritis. The distribution of pain and sensory disturbances varies with the particular nerve root or roots involved. Relief of the acute symptoms usually follow splinting of the neck either with a Thomas collar or with constant head traction using a Sayre's sling. Heat in the form of hot fomentations is helpful in relieving painful muscle spasm.

Shoulder Pain.—Because shoulder pain is a symptom of many local and distal lesions the clinician must be constantly on guard lest he misinterpret the symptoms. Arthritis, fractures, dislocations, muscle and tendon strain or tears, and lesions causing diaphragmatic irritation must

all be considered in the diagnosis and treatment of the painful shoulder. For most rheumatic diseases involving the shoulder, certain principles of therapy have been proven to be of value in the relief of pain and the restoration of motion. During the stage of acute symptoms hot fomentation applied locally offers great relief of pain and muscle spasm and permits freer motion. The shoulder should be put at rest and maintained in a position of abduction and external rotation. Particular stress should be placed on the importance of beginning motion as soon as possible after the acute pain subsides, because adhesions form quickly and a "frozen shoulder" may result. To prevent deformities in the shoulder joint, Joplin and Baer[6] suggest that the patient sleep on a firm bed without a pillow and be taught to lie with his hands clasped beneath his head for short periods several times a day.

Recently Steinbrocker[9] has claimed excellent results with the local infiltration of 1 to 5 c.c. of 2 per cent procaine in oil repeated at three to five-day intervals. The analgesic solution acts to interrupt the sensory reflex arc and in many patients relief of pain is sustained for long intervals after the anesthesia has disappeared. Subacromial bursitis, one of the most common causes of painful shoulders, usually begins with sudden onset of pain most intense at the point of the shoulder. This pain may be so severe that narcotics fail to relieve it. The experience of many investigators has been that the injection of 20 c.c., 2 per cent aqueous procaine into and about the inflamed bursa gives immediate relief.

Extremity Joint Pain.—The joints of the extremities are subject to many types of arthritis and related diseases of which acute rheumatic fever, rheumatoid, hypertrophic and gonococcic arthritis and gout are clinically the most important. The acutely inflamed articulations of rheumatic fever can be easily controlled by putting the patient to bed, protecting the affected extremities by padded splints, applying oil of wintergreen liniment locally and administering large doses of sodium salicylate by mouth.

Throughout the course of rheumatoid arthritis the one symptom most frequently responsible for incapacitation is joint pain. Nevertheless, the systemic nature of this disease must be remembered at all times and treatment must be directed to the patient as a whole rather than to the painful joints alone. There are certain general measures of proven value which all investigators agree constitute the backbone of therapy. Rest, both general and local, efforts to maintain optimum nutrition, physical therapy for the prevention and correction of deformities, and the use of iron for any associated hypochromic anemia are fundamental in the management of this generalized disease. In some cases the removal of diseased tonsils or teeth is advisable. Gold salts, vaccines and vitamin D in massive doses are other measures aimed at arresting the activity of the disease and their use under carefully controlled conditions is advised.

The aim of local measures in the care of rheumatoid arthritic joints is to keep them as free from pain as possible, to prevent flexion deformities and to maintain normal motion. The use of plaster molds gives rest and support during the acutely painful stages and are oftentimes indispensable in the prevention of deformities throughout the course of the disease. These splints may be worn constantly during the acute stage, but should be removed at least once daily to allow motion. Physical therapy in the form of hot poultices, melted paraffin baths, hot and cold contrast baths and baking lamps are comforting, useful aids in the control of joint discomfort, and their frequent home use should be incorporated in the program of therapy.

Hypertrophic arthritis often causes changes in the joints of the extremities and is especially prone to occur in the ankles, knees, hips and the terminal interphalangeal joints of the fingers. In this disease pain may extend for considerable distances into the periarticular tissues. The general measures of treatment are aimed at relieving excessive trauma; reduction of weight in the obese patient may completely relieve the symptoms. The local treatment of the joints with dry heat and massage to increase the blood supply effectively relieves pain.

Gonococcic arthritis is unquestionably less frequent since the introduction of sulfonamide drugs, but it is important to recognize early and adequately treat because crippling deformities can thus be prevented. The gonococcic joint is hyperemic, swollen, hot and exquisitely tender. It has been proven that the use of either sulfanilamide or sulfathiazole in adequate doses (4 to 6 gm. or more per day) until the temperature is normal for forty-eight hours will sterilize an

infected synovial fluid within twenty-four to seventy-two hours. If chemotherapy is unsuccessful fever therapy may be employed. The combination of fever and chemotherapy has been favored by some.

Gout usually causes acute pain in the joints of the extremities, but is usually undiagnosed because most physicians never think of it, or else dismiss it as a disease that is extinct. Gout is not a rare disease, but the recognition of it is rare. In a large percentage of cases its presence can be suspected from the history of repeated attacks of knifelike joint pains limited to one or two joints. Each episode of acute pain is accompanied by swelling, redness and incapacities lasting from three to seven days. The speed of the onset of the pain is a helpful point in diagnosis, for in no other type of arthritis does it develop so abruptly. Usually the painful attacks of gout can be dramatically controlled by the alkaloid colchicine in 1/120 gr. tablets every hour or two hours until 12 to 15 tablets have been administered. This drug is of no value in the control of pain in any other type of joint disease. Until the effect of colchicine is obtained hot or cold compresses and either codeine or morphine may be required for comfort.

Spine and Low Back Pain.—In rheumatoid arthritis of the spine (spondylitis rhizomelique) continuous dull aching pain along the spine, which is increased by motion, coughing, sneezing, or taking a deep breath is characteristic. We have been favorably impressed by the striking improvement which follows roentgen therapy in this one type of arthritis. Treatment is directed over the spine and sacro-iliac joints in divided doses, from 100 to 200 r. at each application. Our results in over forty cases, reported elsewhere,[8] indicate that in fully 80 per cent dramatic relief of pain and stiffness is obtained and in some of the early cases all symptoms are controlled. Hare[4] has reported similar results. Although it is too early to make final evaluation of roentgen therapy, it appears to be of real value in controlling the symptoms in this group of patients.

The number of patients with painful affections of the lower back is astonishingly large and their management is one of the most baffling medical problems. Smith-Peterson[7] differentiates three types of pain resulting from lesions in the lower spine and sacro-iliac joints: local pain, referred pain, and pain due to muscle spasm. In patients with acute low back pain the position of hyperextension obtained either by having the patient lie on his back with a pillow or blanket under the spine, or by having him lie face down will relax the structures and greatly relieve the pain. After four or five days, when the patient is permitted to be ambulatory, protection of the low back by adhesive strapping applied in the position of extension is valuable. Throughout the acute stage additional relief of pain can be obtained by the local application of heat and the use of analgesic drugs.

Summary

Pain is an important factor in incapacitating patients with acute joint disease and in the production of deformities in chronic joint disease. The basis for pain in joint diseases has been discussed and the importance in differential diagnosis has been emphasized. The control of this important symptom constitutes one of the major problems in the treatment of arthritis and allied disorders. Satisfactory analgesia can usually be accomplished by the proper use of rest, splints, drugs, roentgen irradiation therapy and other physical measures.

References

1. Adrian, E. D.: Impulses produced by sensory nerve endings. J. Physiol., 62:33-51, 1926.
2. Freund, H. A., Price, A. E., Steiner, G., and Leichtentritt, B.: Peripheral nerves in chronic atrophic arthritis. J. Lab. and Clin. Med., 27:1256-1258, (July) 1942.
3. Gasser, H. S.: Conduction in nerves in relation to fiber types. A. Research Nerv. and Ment. Dis. Proc., 15:35-59, 1935.
4. Hare, H. F.: The diagnosis of Marie-Strümpell arthritis with certain aspects of treatment. New England J. Med., 223:702-705, (Oct.) 1940.
5. Heinbecker, P., Bishop, G., and O'Leary, J. L.: Pain and touch fibers in peripheral nerves. Arch. Neurol. and Psychiat., 29:771-789, (April) 1933.
6. Joplin, R. J., Baer, G. T.: Treatment of arthritic joints. J.A.M.A., 118:937-944, (March) 1942.
7. Smith-Peterson, M. N.: Personal communication.
8. Smyth, C. J., Freyberg, R. H., and Lampe, Isadore: Roentgen therapy for rheumatoid arthritis of the spine. J.A.M.A., 117:826-830, (Sept.) 1941.
9. Steinbrocker, Otto: Local injections and regional analgesic with procaine solutions for intractable pain in chronic arthritis and related conditions. Ann. Int. Med., 12:1917-1939, (June) 1939.

MSMS

Transfusion accidents may be better investigated if a few cubic centimeters of the transfusion fluid is left in every bottle for at least twenty-four hours.—W. S. Reveno, in *Detroit Medical News.*

Early Unfavorable Responses to Sulfonamide Derivatives Upon Second Administration

By Leonard M. Folkers, M.D.
East Lansing, Michigan

B.S., M.D., University of Iowa, 1932; Intern, Charity Hospital, New Orleans, 1932-33; Senior intern, internal medicine, University of Iowa, 1933-35; Examiner, Student Health Department, University of Iowa, 1935-39; Instructor in Hygiene, University of Iowa, 1937-39; Assistant Physician, Michigan State College Health Service, 1939 to present; Associate Professor in Medicine and Director, Department of Student Health, University of Alabama, 1941-42; Visiting Staff, Sparrow Hospital.

Reactions to sulfonamides usually take the form of fever and rash beginning eight or nine days after more or less continuous use of the drugs. Two cases are reported in which sulfonamide-sensitive individuals were given the medication with early reactions of high fever, nausea, vomiting, erythema, petechial hemorrhages and prostration in one and increased malaise and high fever in the other. Increased use of the drugs may result in frequent reactions of this type but careful attention to a past history of sulfonamide therapy will help prevent similar episodes.

■ College health services with large numbers of upper respiratory infections and their complications have offered an excellent ground upon which to observe the good results given by the sulfonamides in treatment as well as an opportunity to observe the unfavorable reactions incident to their use. The liberal use of these drugs over a period of three and one-half years in a clinic averaging 45,000 calls per school year saw occasional unfavorable reactions of the type usually described, *i.e.*, fever and rash appearing after eight or nine days of more or less continuous use of the drugs by mouth. Two recent cases brought out the possibility of early unfavorable reactions, a condition not previously encountered in patients receiving the drug at the clinic for the first time or after having been given a course earlier. Reports of this type of reaction are not numerous, and, judging from the experiences here, the early unfavorable reactions are not nearly so frequent as the rash and fever on the eighth or ninth day. Nelson[1] reports a case of acquired sensitivity to various sulfonamide derivatives and demonstrates the prompt febrile reaction well. The two cases reported now demonstrate similar problems.

Case 1.—E. C., a white man of twenty years, was admitted to the hospital on January 17, 1942, because of an upper respiratory infection which had progressed to a pneumonic condition of the right lung. The day following admission sulfadiazine was started with two doses of thirty grains each at four-hour intervals and followed by fifteen-grain doses at like intervals. An analysis of the temperature curve (Chart 1) showed

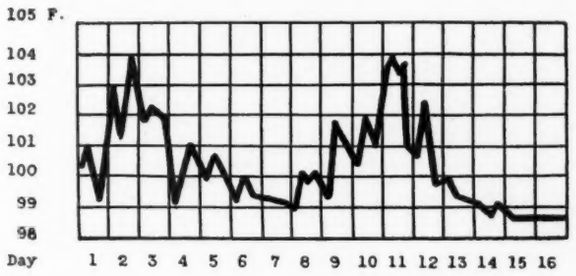


Chart 1. Case 1.

that the admission temperature of 100.4 F. continued to rise until the temperature was 104 F. on the second day at 8:00 p.m. The trend of fever from that time was downward, reaching 99 F. on the eighth day of illness with the clinical course of the pneumonia that of improvement. On the ninth day the fever was elevated again and continued to rise to reach 104 F. on the morning of the eleventh day of illness, when there was severe headache, malaise, nausea, pharyngitis, mental confusion and the appearance of rash over the entire body. The sulfadiazine was stopped and intravenous fluid (3,000 c.c. 5 per cent glucose in saline in twenty-four hours) was given. Edema of the face, hands and feet associated with pruritis was present the following day but the fever began to drop immediately, reaching normal on the fifteenth day. Late on the fourteenth day, without exacerbation of other symptoms or findings, the patient complained of pain and tenderness of the right ear and this progressed to an acute otitis media requiring paracentesis on the fifteenth day. The laboratory findings of this illness showed an admission white blood cell count of 9,600 which decreased to 4,950 on the day of the appearance of the drug rash. Urinalysis throughout the illness was normal.

This same individual was seen in the outclinic one year later, January 16, 1943, at approximately 10:30 a.m. complaining of an upper respiratory infection characterized by moderate pharyngitis, marked postnasal drainage, rhinitis and malaise. There was no fever. Local treatment plus sulfadiazine, grains fifteen every four hours, was instituted and the first dose of this drug was taken at approximately 11:00 a.m. The patient became ill at work about one hour later, developing nausea, vomiting and pronounced weakness. On admission to the hospital at 2:20 p.m. these symptoms persisted and in addition a fever of 102.4 F. was illness with the clinical course of the pneumonia that of improvement. On the ninth day the fever was elevated again and continued to rise to reach 104 F. on found (Chart 2). An hour later the skin over the entire body was flushed and the pharyngitis appeared much worse. The extreme exhaustion was a very prominent feature. Intravenous fluids and codiene gave

some benefit by decreasing nausea and restlessness. Vomiting continued intermittently and the fever remained high. Because scarlet fever was not completely eliminated as a diagnosis and because the history of previous sensitivity to sulfadiazine had not been ob-

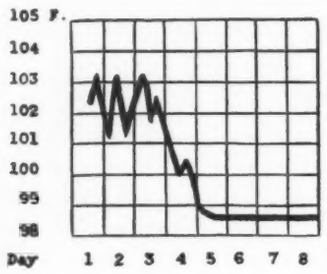


Chart 2. Case 1.

tained, the continued use of that drug was deemed advisable. Fifteen-grain doses every four hours were continued. Nausea prevented retention of any of the drug until 1:00 a.m., approximately twelve hours after admission. Four hours later the medicine was refused because of nausea but thereafter, each four hours fifteen grains were taken with a total of 135 grains being accepted over a period of approximately forty hours, at the end of which time the blood sulfadiazine level was 7.84 mgms. per 100 c.c. Throughout this entire period the patient remained very toxic, being listless, occasionally disoriented and having fever of 103 F. Vomiting persisted. The skin and mucous membrane flush became more severe, being most prominent on the chest, the under surfaces of the arms and in the throat. Forty hours after admission edema of the extremities developed, later involving the eyelids. (6,000 c.c. 5 per cent glucose in saline intravenously during this period.) At this time petechial hemorrhages began to appear through the flush. Within twelve hours of the discontinuance of the sulfadiazine the general condition of the patient had improved remarkably. The temperature dropped to 101 F. and reached normal at about midnight on the fourth day of illness, approximately thirty-six hours after the drug had been discontinued. Except for a continued severe pharyngitis and the appearance of ulcerations of the mucous membrane of the mouth the recovery was uneventful and the patient was discharged on the twelfth day. On admission there was a white blood cell count of 11,350. Succeeding days showed decreases to 8,650 and 6,900, respectively. The original urinalysis was normal but a sample on the third and fourth days of illness gave albumin and many red and white blood cells. Thereafter it was normal. A chest radiograph showed a normal condition.

Case 2.—M. W., a white woman of about eighteen years, was admitted to the hospital in December, 1942, for the treatment of an upper respiratory infection characterized by severe pharyngitis, bronchitis, fever of 102 F. and malaise. In addition to local measures sulfadiazine, grains thirty, every four hours for two doses followed by grains fifteen at similar intervals, was prescribed. Within eighteen hours after the first dose of the drug a generalized rash over the trunk appeared and with the removal of the drug the rash

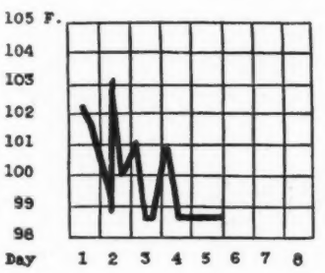


Chart 3. Case 2.

disappeared within another 24 hours. Without any fever exacerbation the recovery was uneventful. In connection with this illness an admission white blood cell count of 7,550 decreased to 5,750 on the third day of illness. The urine was always normal.

This same individual was admitted to the hospital the evening of February 11, 1943, because of a similar illness, with a fever of 102.2 F. Conservative measures reduced the fever to 100 F. (Chart 3) the following morning, but the pharyngitis was becoming worse. Unaware of her sensitivity, a physician ordered sulfadiazine, grains fifteen, given every four hours. This was started at 10:00 a.m. on the second day of illness. Two hours later the patient complained of increased malaise and headache though the fever was only 98.8 F. Another dose of sulfadiazine was given at 2:00 p.m. At 3:30 p.m. the fever was 103.2 F. Questioning revealed the story of sensitivity; the drug was promptly withdrawn and, though the general discomfort persisted throughout the night, the patient was much better the following day. No rash appeared. The fever gradually subsided and the patient was discharged on the fifth day. In connection with this illness the white blood cell count was 6,800 and the urinalysis normal.

Comment

Acquired sensitivity to sulfadiazine used in the treatment of upper respiratory infections in both these individuals undoubtedly was the cause of the unfavorable response to the drug in each patient. Case one presented the typical picture of fever and rash on the seventh and eighth days after the original use of the drug. One year later the re-administration of the same drug produced an immediate unfavorable reaction with symptoms of prostration added to the characteristic phenomena.

Case two presented rapidly appearing unfavorable responses to sulfadiazine on two occasions,

(Continued on Page 828)

President's Page

Another Year

As we begin another year in the life of the Michigan State Medical Society, I want to send greetings to the 1851 medical men of Michigan who are now in our armed forces. I want you to know that we are thinking of you, and our fervent prayers are that this global war will soon terminate in victory for us. Then you can return to your homes and loved ones and again join your friends in the State Medical Society.

To the members who remain in Michigan and who are doing double duty at present. I extend my greetings. My thoughts are of you and I wonder if you are taking a careful inventory of your own health. Do you, yourself, have periodical physical health examinations? Are you getting sufficient rest? Do you regularly get away from the strenuous practice of today and seek a little recreation? These things you owe not only to yourself and family, but to your patients as well. By checking our own health and keeping physically fit, we can best serve our country.

C. R. Keyport

President, Michigan State Medical Society

EDITORIAL

THEY NEVER SLEEP

■ There is a war to be won. No one knows that better than the medical profession. No profession has been called upon for greater sacrifices, and none has responded more generously. While this great task is being carried out we must allow nothing to stand in the way of its accomplishment. This means that not only must we care for the soldiers and sailors, the men in uniform in every part of the world and give them the best care that is known, but we must also give the same case to those left at home, the civilians, the war workers, the families of those doing our fighting. This we are ready to do, and are doing. One-third of our doctors are now in service, and more are being called. Those doctors of medicine who have been left at home are working as never before to do their own work and that of their fellows who are away.

But while doing this tremendous service we are being faced with a threat to our very existence as we know the practice of medicine. While the war efforts are taking our time and last morsel of strength, there are people who wish to change the ways of the world. This program has been threatening for some time, but NOW seems to be an opportune time to do something. The Wagner-Murray-Dingell bill has been introduced into Congress to take over the practice of medicine, and to run it by bureaucrats, administrators, lame ducks, social workers, planners for the future. The people will be relieved of all their cares, including the choice of their own physician and the arranging with him for his services which is an American right not all wish to lose. This program is set up as a great social service that some paternalistic administration is to dole out to the needy, public, under the guise of Social Security, and at the cost of the government, but which will take untold percentages from all our incomes.

Will the doctors calmly submit to this invasion of their time-honored way of practice? Will the government be able to take over the practice of medicine as set forth in Senate Bill 1161? This can be determined by a little flier in paternalistic practices, which again may be done under the guise of altruistic service. Maternity and infant care service can be given to the wives of men in the military services. No one will object to that care, in fact it should be made available to these men and their wives. This service was planned and made available through grants from the Children's Bureau of the Department of Labor. It was an attractive gesture, and many of our doctors accepted it because this was a means of getting some pay for a service to wives of soldiers, sailors, marines and coastguardmen, some of whom may not be able to pay anything except bare subsistance with the salaries they are able to earn in the military services. The Government called them to duty, but made no provision for this added expense. It was a just and proper help to give, but the method of giving was ideally designed to test the possibility of the government invading the practice of medicine, and taking it over for administration by bureaucrats, administrators, and others interested in furthering paternalistic social service.

If this invasion of the practice of medicine can be carried out successfully, a good first step will have been made to make the Wagner-Murray-Dingell Bill more easily workable. If we accept a first invasion of our rights we will be in very much poorer position to resist a further invasion, and then a complete taking over of the practice of medicine. *Other nations have gone through this socialization of their governmental structure and have found the most effective method of accomplishing that end has been through medical service to the people. History shows it always has been the FIRST step to general socialism.*

The method of procedure is insidious. Publicity is secured concerning the need for medical services (especially to the needy wives of our men in the military services), a need that strikes at the very heart strings of us all. But if the doctors ask some consideration in the planning of this service with which they heartily sympathize, they are accused of obstructing the war effort. Michigan's doctors of medicine have made a very workable suggestion to carry out this service in a truly American way, that is, to give these women a subsidy that they can use for their

own care, but this is not even considered by the bureau in charge because "some of these women might not use this money to pay their doctors." The Doctors do not need a subsidy for this work. They would be glad to be paid for their services, but are willing to make their arrangements with their patients the same as they are doing in all the rest of their practice. They do not need or want a bureaucrat between them and their patient, asking questions their patients have a right to consider as personal and privileged. The American method of practice had been acceptable, and has given us the most healthy nation, the lowest mortality rates in the world.

This project has been accepted by some of our states, and rejected by others. The House of Delegates of the American Medical Association rejected it, suggesting an alternate and a workable plan. Now we are hearing rumblings of criticism against the medical profession. *"They are obstructing the war effort!"* Some national organizations that have the ear of the public are whispering that the doctors are not coöperating to win the war. This summer at a meeting of a medical society of Michigan, a Regular Army Colonel, Medical Corps, refusing to be quoted, and saying he was speaking off the record, said this plan was approved and being put into operation by a department of the government, and that was all he wanted to know; it was not his function to question the measure, but the doctors better accept it or otherwise they would place themselves in the position of obstructing progress and the war effort.

No group more than the medical profession wants to win this war and get back to a normal life. Those in the services want to come home, and those at home want them back to take over part of the home front task that is now probably much more exacting and taking a bigger toll of those engaged than the military services. In saying that, we speak from experience. During the period of stress we are exerting every effort of which we are capable to win the war and the peace. And important is the winning of the peace. It is not disloyal to strive to preserve for the American people the plan of medical services and distribution that has placed America where she is in health and mortality matters. No other philosophy of medical practice has ever produced such a healthy nation. We believe in what we have. We know there are adjustments that should be made and we are making them. A medical evolution is now in process. Michigan has been a leader in prepayment medical services, and now many states are evolving such plans. The Beveridge Plan of England saw some advantages in coöperative plans that have been tried, but the Delano plan of America sees nothing good in anything not sponsored by the government. The Wagner-Murray-Dingell bill will pay the doctors of medicine $600,000,000.00 for taking care of the people, and will pay laymen, bureaucrats, lame ducks, politicians one dollar for every dollar paid to the doctors to supervise those doctors.

All these plans and schemes to take control of medical practice and the medical profession are pointed to destroy the private practice of medicine in the United States. *They shall not pass!* There is no more important effort for us to make. We must talk to our patients, to the public. We must mould public opinion which some are trying to prejudice against us. We must VOTE. We must if necessary, play politics, as our detractors are doing, and prove to the public that American medicine is a friend, has been a most worthy friend, and will be hamstrung and thwarted if placed under such hampering restrictions as now threaten. This is not a job for "George," but for YOU. We must all, every one of us, do our utmost to stay this recurring menace.

Federal bureaucracy must be curbed before democracy is killed in our beloved "land of the free." The invaders of state rights must be cast out.

POSTGRADUATE MEDICAL TRAINING

■ There have been so many rapid advancements in methods of raising an army, training it, and providing for the future that, in spite of the great disruption of all civilian and all normal life programs, there have been many things done from which we will receive definite and profound benefits. The training of doctors is one instance. The method of selection for entrance into practice has yet to prove itself, but the training of young doctors, and older ones after they have been commissioned in the armed forces is to be commended. A great number have been sent to special schools and given very substantial and very valuable training, in surgery, medicine, aviation medicine, tropical diseases and many

other special skills that will be necessary to render the very best possible care to the military; and any service that is now valuable to the armed forces will later have its value in private practice. In the other war a great many of our doctors came out of the experience much better doctors, and the advantages of schooling, and postgraduate study were quite limited. This time those advantages are liberally distributed.

The Michigan State Medical Society is also making plans to further opportunities and facilities for postgraduate medical education in an effort to rehabilitate these men in general medical advances, some of which they will have missed in the service.

BUY WAR BONDS

■ The third war loan drive is on. It is not necessary to ask our members to buy WAR bonds. We all recognize the need for funds to prosecute the war, and have been buying bonds, but another reminder is not out of order. Taking a hint from another great organization why not, while we are buying bonds, get one for the Michigan State Medical Society Foundation for Postgraduate Medical Education? The Diocese of Lansing, of the Catholic Church, has suggested that its members have a bond made out to themselves and the Bishop of the Diocese, and send that bond to the diocesan headquarters. It is a good suggestion, and could be copied to advantage by our members. That would help furnish funds for the war, and later a contribution to the Postgraduate program.

EARLY UNFAVORABLE RESPONSES TO SULFONAMIDE DERIVATIVES UPON SECOND ADMINISTRATION

(Continued from Page 824)

one taking the form of the rash, the other producing a high fever within a short interval after the administration of the drug.

If experience shows that unfavorable responses to the sulfonamides have any increased tendency to occur rapidly after the administration of the drugs in a sensitive individual, then reëmphasis must be placed upon two precautions originally brought to the attention of the medical profession when the drugs were first introduced. (1) Careful inquiry regarding the previous use of a sulfonamide or an unfavorable reaction to the drug must be made before re-administration of a similar drug. (2) Sulfonamides are best given to patients confined to bed, preferably in hospitals under adequate supervision. To permit patients to suffer added days of incapacity as a result of drug therapy is inadvisable in a nation requiring all available manpower. Likewise, if prostration is to be a prominent symptom in the cases responding unfavorably, then patients must be warned to remain away from active machinery and the like as long as the possibility exists.

A decrease in the white blood cell level accompanied the unfavorable responses in both reported cases and would seem to be a valuable guide to the anticipation of later trouble. If this significant decrease be found regularly during the original course of therapy, even though other symptoms of toxicity do not develop, sulfonamides might be better withheld in the treatment of most later conditions.

Edema of parts of the body was a finding in both episodes in Case one. Remaining to be solved is the question of whether this was a feature of the response in a highly sensitized individual or was the result of a body chemistry disturbed by vomiting and intravenous fluids. On neither occasion was the fluid intake excessive and, though kidney irritation did exist during the second illness, it was of short duration.

Summary

Two cases of an immediate unfavorable response to sulfadiazine therapy in individuals previously having demonstrated a sensitivity to the drug are reported. The liberal use of sulfonamide drugs in therapy of many ailments makes it likely that the responses of this type will increase in number. Careful attention to a past history of sulfonamide therapy will help prevent similar episodes.

Reference

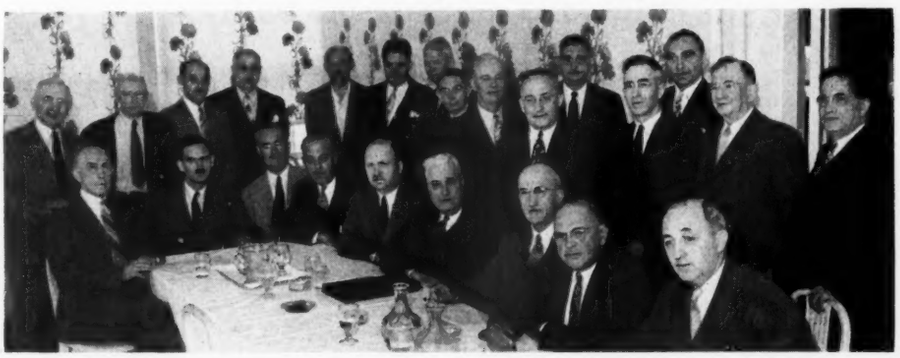
1. Nelson, Jack: Acquired sensitivity to sulfonamide drugs. Jour. A.M.A., 119:560, (June 13) 1942.

MSMS

Restoration of gray hair to its natural color by vitamins has failed in humans, judging by the absence of significant change in hair color in seventeen of nineteen elderly people subjected to intensive treatment for eight consecutive months.—W. S. Reveno, in *Detroit Medical News*.

MEDICAL AND HOSPITAL EXECUTIVES OF MICHIGAN MEET

Unprecedented in the history of Michigan was the joint meeting of executives of the Michigan State Medical Society and the Michigan Hospital Association held on July 17. An important program of joint activity and endeavor, to which officers of Michigan Hospital Service and Michigan Medical Service also subscribed, was outlined by spokesmen and referred to a Joint Committee created as a result of the meeting. Such a harmonious joining of forces, to solve mutual problems, will attain positive good for both professions and for the public which they serve. The movement which had its beginnings in Michigan in July is being watched with interest by a number of other States, with a view to emulating this progressive step.



Left to Right (Seated)—A. H. Miller, M.D., Gladstone; J. C. Ketcham, Detroit; R. S. Huston, Flint; O. O. Beck, M.D., Birmingham; O. D. Stryker, M.D., Fremont; R. S. Morrish, M.D., Flint; D. W. Myers, M.D., Ann Arbor; President C. R. Keyport, M.D., Grayling; C. E. Umphrey, M.D., Detroit;
(Standing)—T. E. DeGurse, M.D., Marine City; R. G. Greve, Ann Arbor; E. F. Sladek, M.D., Traverse City; Wilfrid Haughey, M.D., Battle Creek; W. H. Huron, M.D., Iron Mountain; J. R. Mannix, Detroit; Graham Davis, Battle Creek; W. J. Griffin, LL.B., Detroit; V. M. Moore, M.D., Grand Rapids; L. Fernald Foster, M.D., Bay City; L. V. Ragsdale, M.D., Grand Rapids; P. L. Ledwidge, M.D., Detroit; W. A. Hyland, M.D., Grand Rapids; W. E. Barstow, M.D., St. Louis; and A. S. Brunk, M.D., Detroit.
President H. H. Cummings, M.D., Ann Arbor; and Councilors R. J. Hubbell, M.D., Kalamazoo; R. C. Perkins, M.D., Bay City; and P. A. Riley, M.D., Jackson, were not present when the photograph was taken.

The minutes of the Council of the Michigan State Medical Society graphically describe the momentous joint session of July 17:

MSMS Council Chairman Brunk introduced L. V. Ragsdale, M.D., Michigan Hospital Association President, who in turn presented Graham Davis, immediate Past-President; R. G. Greve, Secretary; R. S. Huston of the Board; J. C. Ketcham, Executive Vice President of Michigan Medical Service; W. J. Griffin, President, and J. R. Mannix, Director, Michigan Hospital Service.

M.H.A. President Ragsdale thanked Dr. Brunk for arranging this meeting of the Hospital group with the Council. He stated that for some time he had felt that the Michigan Hospital Association needed the help and advice of the Michigan State Medical Society. Further he thought that the advice and support of the Michigan Hospital Association could be of help to the Michigan State Medical Society. He stated that the proposed changes in the Federal Social Security Act to include hospital benefits would destroy our present volunteer hospital system and would sound the death knell to our Blue Cross plans. The Hospital group needs the help of the Medical Society in converting such legislation.

Dr. Ragsdale stated that there would be a need of full utilization of our existing hospital facilities for an expansion of our graduate teaching program during the immediate postwar period. More residencies must be provided for the younger physicians who were called into service as soon as they completed their one-year rotating internship. Many older staff men in the service must be provided with graduate courses to prepare them for reëntering civilian practice. Our Hospital Association can and should help with this program. He cited the Bureau of Maternal and Child Health program as an example in which coöperative action would be of great value.

He stated that the Medical Society could be of great help in the Hospital Survey which the Michigan Hospital Association is undertaking this year, and the Michigan Hospital Licensing Law which the Hospital Association hopes to sponsor at the next session of the Legislature. Dr. Ragsdale ended by saying, "These are only a few examples of problems in which the two organizations are mutually interested. We should pool our efforts in solving these problems and to that end I suggest a Joint Study Committee, composed of members from The Council, Michigan Hospital Association Trustees, Michigan Medical Service and Michigan Hospital Service."

Each of the hospital delegation then was asked to comment and each spoke briefly telling the need of such a Joint Committee.

Graham Davis presented facts on the hospitals of the state, and further amplified the need for a hospital survey and for a hospital licensing law.

Mr. Griffin presented the relationships between the medical and the administrative sides of hospitals.

Mr. Mannix spoke of the work being done by the Public Health League of California; also the dangers and scope of the new Wagner-Murray-Dingell bill, and the need for coöperative activity between the medical and hospital groups.

Mr. Ketcham spoke in behalf of Michigan Medical Service and its progress, and the coöperation it has received from Michigan Hospital Service.

Messrs. Greve and Huston expressed their pleasure at being present at this important joint session.

Dr. Haughey felt there was great need for joint action of the medical and hospital groups, particularly in defeating the Wagner bill and other similar schemes.

President Cummings stressed the value of coöperation and the hope that joint endeavor of the groups represented at this meeting could be instituted at once through the formation of a Joint Study Committee, as recommended by the Michigan Hospital Association through its President Ragsdale.

Motion of Drs. Morrish-Barstow that the formation of a Joint Study Committee be approved (three representatives from the Michigan State Medical Society, three from the Michigan Hospital Association, two from Michigan Hospital Service, and two from Michigan Medical Service) and that three Doctors of Medicine, as Michigan State Medical Society representatives, be appointed to serve on this committee for the purpose of mutual coöperation. Carried unanimously. Committee: A. S. Brunk, M.D., W. E. Barstow, M.D., and C. E. Umphrey, M.D.

The representatives of the Michigan Hospital Association, Michigan Hospital Service and Michigan Medical Service were thanked for their attendance at the Council meeting.

WHO MAY PRESCRIBE DRUGS

Osteopaths have no general right to administer or prescribe drugs for internal human medication.

The right to administer drugs does not come within the definition of chiropractic.

The above clear-cut opinion was handed down by Herbert J. Rushton, Attorney General of Michigan, on September 16, 1943. The complete text of the Attorney General's opinion, addressed to the Office of Price Administration, Detroit District Office, Attention of Harlan P. Cristy, Chief Rationing Attorney, follows:

We have your inquiry as to what persons are licensed by the law of this state to prescribe drugs for internal human medication.

You assume, and correctly so, that the license to practice medicine and surgery would authorize the holder to prescribe all drugs for internal human medication. You include "homeopaths" in your list of those engaged in the various branches of the healing arts. The homeopathic theory of medicine is embraced within the general Medical Act of this State and those who follow the theory of homeopathic medicine are accorded all the privileges provided in the act in relation to the practice of medicine.

In Michigan the licenses to practice the various branches of the healing arts are confined to the practice of medicine, osteopathy, and chiropractic. There is also provision in the Medical Act for the issuance of a license to so-called "drugless practitioners" who of course do not have the right to administer medicine. There is no license provided in our law for the practice of "naturopathy." There are of course those engaged in limited fields of healing such as chiropodists and optometrists. Neither of these groups may administer medicine for internal use. I might add that the practice of nursing does not authorize the licensee to administer drugs except under the supervision and direction of a physician.

As to the practice of chiropractic, Section 6 of the Chiropractic Act, Act 145, P.A. 1933, defines chiropractic as:

"Sec. 6. The license provided for in this act shall entitle the holder thereof to practice chiropractic in the State of Michigan, and for the purpose of this act chiropractic is defined as 'the locating of misaligned or displaced vertebræ of the human spine, the procedure preparatory to and the adjustment by hand of such misaligned or displaced vertebræ and surrounding bones and tissues.'"

The right to administer drugs does not come within the definition of chiropractic.

Osteopaths have no general right to administer or prescribe drugs for internal human medication but they may administer narcotic drugs for temporary relief of pain.

Very truly yours,

HERBERT J. RUSHTON
Attorney General

JOHN R. DETHMERS
Chief of Assistant Attorney General

TUBERCULOSIS CASE FINDING

Because of the war and the anticipated increase in tuberculosis incident to it, the physician must be more than ever vigilant and on the alert to spot cases of tuberculosis among his patients and in the area of his practice. To help the physician be alert in this task, the Tuberculosis Control Committee has condensed information and instructions on the attached card. Keep it on the office desk for handy reference.

1. The burden of case finding rests with the General Practitioner. Suspect tuberculosis in all uncertain cases.
2. Tuberculosis spreads from persons having the disease. Prevent spread by hospitalizing all known cases.
3. The diagnosis of tuberculosis in the early, curable stage is imperative. Check all known contacts and all suspects.
4. Diagnosing tuberculosis is not difficult. The *history* provides more clues than the physical examination. (Physical signs and positive sputum are found only in advanced stages). *Tuberculin test* all suspects and *x-ray* the positive reactors, or, when possible, use the x-ray primarily. Positive sputum is conclusive.
5. All NEW cases should be considered active until proven otherwise. Send them to an approved sanatorium for a period of observation.
6. Collapse therapy provides the best results in the shortest time. It is most effective in early cases. Hospitalize all cases for the benefit of modern treatment.
7. Education will further decrease tuberculosis deaths—brush up on tuberculosis and help teach people what they should know.

Tuberculin Test

1. OLD TUBERCULIN is distributed free to all physicians by the Michigan Department of Health in "Two Strength" or "Single Strength" dilutions for the Mantoux test and as "Tuberculin Points for the Von Pirquet test. Complete instructions are enclosed with each preparation. Obtain fresh supply from local department of health.
2. P.P.D. (Purified Protein Derivative) Tuberculin is sold in tablet form with vials of buffer solution and instructions for mixing and giving the test.
3. PATCH TEST (Vollmer). Strips of adhesive tape are impregnated with Tuberculin in the end sections with the central part free for control. They are in sterile packages, ready for application to the cleansed skin surface. Instructions accompany each test strip.
4. A Positive Tuberculin Test means that tuberculous infection has occurred but not necessarily that tuberculous disease has developed. It calls for an x-ray examination.

X-ray

1. X-ray examination is the only dependable way of detecting early tuberculosis. It gives reliable information regarding the location, extent and character of the disease and a good idea of the probable response to treatment. It is of definite value in differential diagnosis.
2. Use standard technique in making the exposure.
3. For interpretation, send the film to a Roentgenologist or to an approved tuberculosis hospital.
4. Do not hazard a diagnosis on an unsatisfactory film.
5. Report all diagnosed cases to the Department of Health on forms provided.

Hospitalizing a Case of Tuberculosis

1. There is no substitute for modern treatment in a sanatorium.
2. Most patients cannot afford to go to a private sanatorium. Michigan laws provide modern sanatorium treatment at County and State expense.
3. Contact the County Health Officer, who will arrange for admission of the patient to an approved tuberculosis hospital. (If there is no county health unit, contact the Health Officer, city, village, township, county or district.)
4. Follow the case during hospitalization in preparation for managing it after discharge.
5. Tuberculosis can be eradicated—Diligence on the part of the practicing physician is absolutely essential in this fight.

✶ YOU AND YOUR BUSINESS ✶

QUESTIONS AND ANSWERS PERTAINING TO THE RELEASE OF X-RAY FILMS AND REPORTS

S. W. DONALDSON, M.D.
Ann Arbor, Michigan
and B. R. VANZWALUWENBURG, M.D.
Grand Rapids, Michigan

The ever-increasing importance of diagnostic roentgenology has led to increasingly varied requests to the roentgenologist for release of films or of information derived therefrom. Requests for information come from the patient, from his relatives, and from physicians whom he has consulted in addition to the original referring physician. His lawyers, lawyers of persons who have opposing interests in the case, and osteopaths and chiropractors may also request reports or opportunity to view the films. Proper procedure in the release of information is further obscured if the examination has been made at the request of an insurance company which is financially liable in the case and has paid for the examination.

Very few court judgments are available as precedents to indicate correct procedure. This discussion is an attempt to determine from general principles as well as from precedent what the probable court action would be in a given situation.

However, the procedure which will satisfy the bare minimum requirements prescribed by law will not be broad enough to provide release of information in all the situations in which such release is in the best interests of the many persons affected. The further attempt is made, therefore, to define those situations in which release of films or reports is advisable although not required by law. It is hoped that the discussion of these principles, concerning which wide disagreement may be expected, will encourage further thought and lead eventually to greater uniformity of practice. There are three principles involved.

The few pertinent court decisions which have so far been made have been based on *principles of contract.* In determining what the implied contract was between roentgenologist and patient, the courts have relied on common practice as a guide. They have established the identity of the roentgenogram and of the roentgenologist's report as medical records. "In a sense they differ little if at all from microscopic slides of tissue made in the course of diagnosing or treating a patient . . . " (McGarry vs. J. A. Mercier Co., 272 Mich. 501, 262 N.W. 296). In general the decisions have ruled that the implied contract between roentgenologist and patient has been fully satisfied when the roentgenologist has made his examination and communicated his finding to the referring physician.

Legal opinion suggests that, in addition to the contractual aspect, a *principle of equity* might be considered—namely that the patient, as the prime interested party, retains an interest in the results of examination in the sense of a right to beneficial use, although not possessing the right of ownership itself. This aspect has not yet to our knowledge been expressed in court opinions regarding roentgenograms or any other form of medical record. The roentgenologist's prime responsibility is, however, to the patient, and the professional principle of doing that which is in the patient's best interests suggests that a right to use of the information, beyond that required by contract, should in many circumstances be granted.

The *principle of privileged communications* is operative, of course, in this as in any other physician-patient relationship.

Questions and Answers

1. Q.—*Mr. A. requests possession of x-ray films of himself. Is it necessary to grant this?*

A.—No. One of the few questions regarding release of films for which court precedent exists is that of ownership. In the case previously quoted of McGarry

(Continued on Page 834)

vs. J. A. Mercier Co. the court ruled that, in the absence of any special agreement to the contrary, ownership of the films remains with the roentgenologist who has made the examination or hospital where it was made.

2. Q.—*Mr. B. requests, for his own use, a copy of the report of an x-ray examination made of himself at the request of his referring physician. Is it necessary or advisable to grant this?*

A.—Court opinion has not as yet ruled on this question. No written contract is as a rule involved. The implied contract under which the examination was made involved only an examination and a report to the physician who referred the patient for roentgenological consultation. Court interpretation of the implied contract would undoubtedly be influenced by common practice in similar situations and it is not, of course, common practice to deliver roentgenological reports directly to the patient.

As a general rule it is not advisable. A committee of members of the American Roentgen Ray Society recommended in 1914 as follows: "That no report should be given to the patient except through the referring physician or surgeon. That patients are sent for consultation and diagnosis and are not entitled to plates or prints. Prints in the hands of patients lead to false interpretations, confusing opinions, multiplicity of advice and bad results."

3. Q.—*Is Mr. C. to be granted opportunity to view his films?*

A.—In general, no. (See answer to question 2.) The opportunity should be granted however, if desired by the referring physician. In some cases discussion of the films with the radiologist will increase the patient's coöperation or morale. In other cases (as in metastatic maligancy or hypochondriasis) it might be very inadvisable. The decision is best left to the referring physician. In special instances, as in clearly demonstrable fractures, the attending physician's assent may be taken for granted and the patient's natural curiosity satisfied.

4. Q.—*Mr. D. has changed physicians. Should the radiologist, at Mr. D.'s request, send a copy of the x-ray report to the new physician and permit him to view the films?*

A.—A recent decision of a California Superior Court ruled that the roentgenologist was "justified in refusing to surrender possession of the x-ray negatives" when the roentgenologist had refused to show the films except on authorization of the referring physician.

It is to be noted, however, that the patient may discharge a physician at any time without explanation and when he discharges the attending physician he does not by doing so discharge all consultants the physician has had in connection with the patient's diagnosis or treatment. The consultant and the patient still remain in a physician-patient relationship. No one can gain by a refusal as it will not improve the relationship between patient and original physician. The patient will certainly gain if the request is granted. Common sense indicates that the patient's right to change physicians would be impugned by refusal to grant this request. Granting this request is apparently not legally mandatory but is considered advisable.

5. Q.—*Should a copy of the report be sent, at Mr. E.'s request, to his lawyer without the referring physician's permission?*

A.—Yes, although according to the California Superior Court decision this also is not legally necessary. The only case in which one of the interested parties might be harmed by such action would be in case the patient were bringing suit against the referring physician. In such a case, if the x-ray evidence were pertinent, the physician could hardly hope to defend himself by keeping this evidence out of court. The legal right of privileged communication is completely in the patient's control and his physician cannot prevent his waiving that right.

6. Q.—*A lawyer representing an insurance company requests opportunity to view Mr. F.'s films. Should this be granted without Mr. F.'s authorization?*

A.—No. The statutory laws of privileged communications require that no information be given out without the patient's permission.

If, on the other hand, the insurance company has paid for the examination the patient may be considered to have given consent to release of information to the company. The Michigan decision indicates that compliance even in this situation is not necessary, the reports to the physician being sufficient to fulfill the contract. As a practical matter, however, failure to make the release, if the insurance company has paid for the examination, is merely obstructive.

7. Q.—*A doctor of medicine engaged by an insurance company which is liable for injuries to Mr. G. has requested an x-ray examination following an accident and the insurance company has paid the roentgenologist's fee. Should a copy of the x-ray report be sent to Mr. G.'s personal physician or lawyer at Mr. G.'s request?*

A.—Yes. Mr. G. is the person primarily concerned in the examination and, in the absence of any agreement to the contrary, has only yielded to the insurance company the right of access to the information derived from x-ray examination. He has not yielded to the company the exclusive right to such information. The courts might rule that such release of information is not necessary. It does not appear that they would rule it improper.

8. Q.—*Should films be released, at Mr. H.'s request, to his chiropractor or osteopath?*

A.—Under contractual law it is not necessary. It would usually be impolitic. Most physicians would consider it unethical.

9. Q.—*Do the statutes pertaining to privileged communications apply to testimony in court?*

A.—Yes. In most instances, however, the patient either by bringing a court action or in some other way, has waived the privilege. Both films and records are subject to subpoena at any time and must be produced when ordered by the court. The question

(Continued on Page 836)

of their admissibility as evidence under the code of privileged communications is then to be decided by the court.

Summary

Summary of the legal and ethical principles involved in the release of x-ray films and reports:

1. When the consultant roentgenologist has made the examination and sent his report to the referring physician he has completely fulfilled his legal contract.

2. "Films or reports in the hands of patients lead to false interpretation, confusion of opinions, multiplicity of advice and bad results" (American Roentgen Ray Society). It is therefore *in the best interests of the patient* that all reports or opportunity to view films come to him through the referring physician or with his permission.

3. The patient has the right to change physicians and does not automatically discharge consultants in so doing. It is therefore *in the best interests of the patient* that access to the reports and films be given at the patient's request to any physician or other person who has a legitimate interest in the case.

4. No one may be given the right of access to films or reports without the patient's permission.

5. Ownership of the films remains with the roentgenologist.

Rules to be established in a roentgenological office or hospital department to govern the release of films and reports according to these principles: 1. Films and reports shall be shown to patients or relatives only at the request of the referring physician.

2. Regardless of who has paid for the examination, films and reports shall be made available to any physician or other person with a legitimate interest at the patient's request.

3. No one shall be given access to films or reports without the patient's permission.

4. All films remain the property of the roentgenologist. Films loaned shall be accompanied by a request for prompt return.

CURARE

Collier's, August 13, 1943, in an article by J. D. Ratcliff, tells about the development of a new drug, curare, the arrow poison used by the South American Indians. A. E. Bennett of the University of Nebraska did the first work with a refined lotion, and so far the work has been entirely on an experimental basis.

Lengthy research and experiments were required before a pure, standardized curare which, when applied to animals and human beings has a paralyzing effect, was obtained for clinical trials. And, since the clinical work began, it has been discovered that the refined curare can be used to:

1. Paralyze muscles prior to the submitting of patients, suffering from dementia praecox and manic depression, to shock treatments which ordinarily had produced convulsions that frequently led to broken bones.

2. Provide relief—only temporarily because it has no healing qualities—to those afflicted with spastic paralysis.

3. Lessen muscular contractions of intestines during operations for such ailments as hernia, appendicitis or some abdominal obstruction.

Moreover, according to Ratcliff, curare offers promise on treatment of tetanus—lockjaw.

AMERICAN-SOVIET MEDICAL SOCIETY CHAPTER LAUNCHED IN DETROIT

The American-Soviet Medical Society, recently organized to stimulate the exchange of medical information between the United States and the Soviet Union, formally launched its Detroit chapter on Wednesday evening, August 18, at a meeting held at the WWJ auditorium. Professor Vladimir V. Lebedenko of the Department of Surgery at the First Moscow Medical Institute, who is at present in the United States as official representative of the Russian Red Cross, was the chief speaker. He described his experiences with Soviet war medicine and particularly with new methods of treating shock at the front.

Dr. Warren B. Cooksey, head of the Michigan Blood Bank, presided. The gathering was addressed by Dr. Barris, head of the Detroit chapter of the American Red Cross; Dr. Bruce H. Douglas, commissioner of the Detroit Board of Health; a representative of the Wayne County Medical Society; and the executive secetary of the American-Soviet Medical Society.

Professor Lebedenko was the guest of the Detroit chapter of the American Red Cross before the meeting and made visits to various Detroit hospitals during his stay there.

MICHIGAN MEDICAL SERVICE

Michigan Medical Service is becoming a very convincing evidence that such measures as Senate Bill 1161, the Wagner-Murray-Dingell bill, are not needed. Michigan was a pioneer in the attempt to render a prepaid medical service to large groups of citizens. At

first our effort met with a good degree of success, but as we expanded and met with adverse coöperation, and adverse experience we lost. At one time there was an actuarial deficit as high as $540,000.00 At the end of the first year of operation there was a profit of about $30,000.00, which turned in to the deficit mentioned. But during this time Michigan Medical Service was learning the hard way many facts entering into the costs of rendering service to large groups of people, and some readjustments in rates and other plans were made. The deficit began to decline in November, 1942, and by July 1, 1943, when the last audit was conducted by a firm of nationally known auditors this had been reduced $227,000.00 There has been a favorable balance every month for eight months, and estimates made since that date show the same tendency, though final figures are not yet possible to obtain.

Where at first it took over sixty days to pass a payment through the routine of analysis and payment, involving at times the waiting for funds the time now is thirteen days, which approaches the minimum, and there is a bank balance sufficient to pay all claims as soon as they are claims, and there was enough in addition so that a handsome sum was invested in war bonds during the Third War Loan.

Many states are now following the plan of prepaid medical services for groups, and making detailed studies. Quite a number of plans are in operation, and they should be successful, for they have had the experience of Michigan and California to draw upon, and have been able to avoid many of the mistakes that we made in ignorance and innocence. Successful prepayment plans in many of the states will go a long way to point the futility of the Senate bill 1161. Michigan has been commended for its pioneer work.

The *West Virginia Medical Journal* for September reports that the State Board of Health, with the approval of the Children's Bureau of the Department of Labor at Washington in the emergency maternal care program for the care of wives of enlisted men, has fixed a fee of $50.00 for the care during prenatal, labor and puerperium, as against the old rate of $35.00. The delivery is fixed at $35.00, other fees accordingly.

Examination of 2,332 white men revealed that the pot-bellied had, on the average, less pneumonia and cancer, and no more diabetes than the willowy and sylphlike. This does not apply, of course, to extremes. Among those examined, the enormous tended to die early, as did the cadaverous; but a modestly aldermanic girth is quite consistent with long life.—Dr. Raymond Pearl, as quoted in *Southern Medicine and Surgery.*

SENATE BILL 1161

Without apology or explanation, a legislator has undertaken to overthrow the practice of medicine. A bill is introduced into the Senate and overnight

doctors of medicine become government property to serve like robots.

Gone is the freedom of enterprise that took doctors to the laboratories in silence and often in poverty, to develop cures for disease. Gone is the incentive that gave the physician a personal pride in his work, an interest in the welfare of his patient. Gone, all this, if the bill becomes law.

At the base am I, the lowly doctor, now offering what drugs a Washington official tells me to use, delivering babies according to the manual of instructions that will be prepared, setting bones with the aid of a chart from the Health Service, identifying measles or meningitis by comparing my findings with color photographs of typical cases.

I work eight hours and I rest at night. The doctor on the night shift follows through while I sleep and I shall be content, the legislator tells me, for the government will send me money for my services, as if that solves my fears.

As if that's why I dressed at two this morning to visit the baby with diphtheria, as if that is why I stayed at the hospital all night with the boy who fell from a tree! And the patient too is happy because he pays nothing for this service. It is free except for what he pays the government. The fact that this is many times the amount he ever paid his doctor should not bother him, we hear, because freedom is expensive. Our government will make him free. And me also, they say.—*The Medical* (Wichita, Kansas) *Bulletin.*

RAPID TREATMENT CENTERS FOR SYPHILIS

In order to clarify the policies and responsibilities of the U. S. Public Health Service in the new nation-wide system of Rapid Treatment Centers for persons infected with venereal disease, a special edition of the "VD War Letter," published by the Division of Venereal Diseases of the Public Health Service, was issued last month. It revealed the following facts:

More than thirty Rapid Treatment Centers will be in operation by the end of 1943. Approximately 15,000 infected persons will be admitted to the centers and rendered non-infectious, their disease either arrested or cured, during the war.

The Rapid Treatment Center program is an outgrowth of the national venereal disease control program begun in 1938, and it has been developed jointly by state health departments, the Office of Defense Health and Welfare, the U. S. Public Health Service, and the Federal Works Agency. It is intended to be "a direct and realistic effort to combat a definite wartime threat to our national strength."—*Ohio State Medical Journal,* April, 1943.

Bureau of Census *life tables* show that the average lifetime of rural people is longer than that of urbanites, women longer than men, and whites longer than nonwhites.

CORRESPONDENCE

H. H. Cummings, M.D., President
Michigan State Medical Society
Lansing, Michigan

Dear Dr. Cummings:

As Director of the Medical-Research, Health and Accident Division of the UAW-CIO, my attention has been drawn to the number of war production workers who are being swindled out of hard earned monies by advertising clinics, sanitariums and such like which profess to be able to cure everything, but which in reality are nothing but unadulterated fakes.

These people, by their deceit and trickery, are not only leeching on the workers' wages, but in so doing are also damaging our war effort. In these times when the health of the worker is of so much importance to the Nation—when it is imperative that all available manpower be kept physically fit to reduce absenteeism and keep the wheels of industry turning, it is alarming that so much quackery is allowed to openly flourish.

A few examples will emphasize the seriousness and the extent to which this deceit is being carried on.

A worker was recently guaranteed to be cured of hernia by injection treatments for $150.00. After paying $90.00 in advance and receiving one injection, an examination disclosed that the worker had no hernia at all.

Another worker was guaranteed the same cure and after paying $145.00 in advance and receiving a number of treatments, an abscess in the site of the injection developed with the result that the worker was out $145.00 in cash, was not cured of the hernia and in addition had an abscess which would require surgical treatment.

A worker visited another of these advertising clinics, and after a fluoroscopic x-ray without the use of barium, was told he had an ulcer of the stomach as big as a half dollar. This was all done as advertised in the press for the sum of $2.00. After the examination, he was given a bottle of medicine for $2.00 and advised to take a series of 15 treatments for $30.00. The treatments consisted of laying heating pads over the chest, which is certainly not accepted as proper medical treatment for ulcers. Examination later disclosed that the worker had a pathological appendix. In other words, the $2.00 ad was just a come on and the clinic was reaping golden harvest in selling medicine and diathermy treatments. In this particular case, the worker spent $34.00 in cash, lost two months in wages and was simply tricked into thinking that he was being completely cured.

These are just a few examples of the fraud and quackery that are constantly being practiced on the workers in this state.

There has also been a very noticeable increase in

advertising cure-alls. Particularly is this true in the advertising of trusses for the cure of hernia. In the first place, it is a well-known fact that the use of a truss will never cure a hernia, yet trusses are constantly being advertised for this purpose at the supposedly sacrificial price of $100.00, while a good or better truss than those advertised can be purchased from a reliable business house for only $10.00.

Advertisements proclaiming wonderful results from patent medicines are also on the increase. These medicines are supposed to cure practically everything and especially female disorders, kidney and liver troubles. All of them are ineffective, and the advertising entirely misleading.

It is deplorable that conditions such as we have stated are permitted to exist within this state. We, therefore, request that the Michigan State Medical Society together with the Wayne County Medical Society make comprehensive surveys and take immediate steps to stop the many trick devices that are being used to lure money away from the workers through false pretenses.

We ourselves have decided to establish a special advisory department in the Medical-Research Institute to work along this same line and will do everything possible to warn our membership to beware of patent medicines and medical agencies that resort to advertising to secure business.

Very truly yours,
(Signed) GEO. F. ADDES
International Secretary-Treasurer

July 1, 1943

* * *

George F. Addes
International Secretary-Treasurer
United Automobile—Aircraft—Agricultural
Implement Workers of America (UAW-CIO)
411 W. Milwaukee Ave.
Detroit, Michigan

Dear Mr. Addes:

Thank you for your kind letter of July 1 which I held for presentation to The Council of the Michigan State Medical Society, at its meeting of July 17.

The Council instructed that congratulations be sent to the UAW-CIO on its efforts to stamp out fake clinics, charlatans, and substandard practitioners.

This problem has been fought by the medical profession of Michigan and by the entire medical profession of the country (notably through the Bureau of Investigation of the American Medical Association) for many, many years. We are cognizant of the vast amount of monies wasted on patent medicines, fake clinics, charlatans, and especially on practitioners of healing who are not qualified by education, training or experience to perform the work they so brazenly attempt to do.

We hope that the labor group will continue its fight against all such "cure-all organizations and people," and bring proper information to its hundreds of thousands of members so that the best of medical care—and only the best—will be obtainable by them. In this commendable program, the Michigan State Medical Society offers you its full facilities and sincere help. In addition, it recommends that you enlist the services

of the Michigan State Board of Registration in Medicine and the Michigan Department of Health, both agencies of state government which have police power. Finally, the State Society offers the recommendation that you use your influence with county prosecutors to see that the Medical Practice Act of Michigan as well as the health regulations of the various communities are upheld.

Please call upon the Michigan State Medical Society whenever we may be of any service to you.

Very cordially yours,

H. H. CUMMINGS, M.D., *President,* MSMS

July 20, 1943

Dr. Wilfred Haughey
610 Post Building
Battle Creek, Michigan

Dear Dr. Haughey:

For the past two years I have been a member of the Michigan State Nutrition Defense Committee as a representative of the State Medical Society. At the last meeting in Lansing, September 15, the committee asked if it were possible to give some publicity in the State Medical Journal to National Nutrition Week, which is to be during the first week of November. I do not know who handles such publicity for the state publication and I am therefore addressing this letter to you. I felt that this mode of approach would be more satisfactory than an announcement at the various county society meetings, since it is more likely to reach men who are now too busy to attend meetings.

You will notice that the entire month of November has been designated as National Nutrition Month. The individual states have been instructed to carry on the campaign throughout the month of November, but to choose one week during the month for its most intensive campaign. The State Nutrition Committee has chosen the first week of November but intends to continue with radio programs, newspaper articles, et cetera throughout the entire month.

September 20, 1943

J. W. CONN, M.D.

There is now in process of preparation a Community Mobilization Handbook which will give suggestions about the further organization of the committees and will contain a list of activities the committees can carry on, which may be adapted to suit any type and size of community. Among the suggestions will be the holding of Nutrition "Weeks" or special Nutrition "Days" during November of the type discussed at the Conference of State Nutrition Committee Chairmen, in any locality where the Committees may wish to undertake such an activity. It would be highly desirable to begin development of other plans for participation in Food for Freedom Month based on information in the booklet.

We know that many of you are already participating in the Home Front Pledge Compaign initiated by the Office of Price Administration and that in some places local nutrition committee chairmen are heading up Citizen Committees set up for that purpose.

THE DOCTOR'S LIBRARY

Acknowledgment of all books received will be made in this column and this will be deemed by us as a full compensation of those sending them. A selection will be made for review, as expedient.

REHABILITATION OF THE WAR INJURED, A SYMPOSIUM. Edited by William Brown Doherty, M.D., and Dagobert D. Runes, Ph.D. Illustrated. New York: Philosophical Library, Inc., 1943. Price $10.00.

A significant start in the rehabilitation of the injured of the war is described in this book. The head injuries are probably first considered in estimating what the problems are to be, but that is only a small part. There are injuries of every part and tissue, and they are pretty well all considered in this book. Many authors and many subjects are listed in a two-page table of contents. Neurological psychiatry, reconstructive plastic surgery, orthopedic care are covered in detail. Hints are given on the methods of amputations so as not to have much shock and many bad stumps. Burns and their treatment, and jaw reconstruction are only a few topics. Physiotherapy, occupational therapy, vocational guidance, and legal problems receive full consideration, and each topic by an expert in that particular subject. Survivors of shipwreck with their vascular and neurologic lesions are discussed by Commander James White. There are 684 pages of real meat for those interested in this subject, and that includes not only those who will be working in the rehabilitation of the war injured, but civil injuries will produce just as intricate cases, and those are deserving and requiring just as much knowledge and skill in their handling. The type is of good size, the paper not too glossy, or thin, yet the book is not too big for reading. The style is that of the fifty-seven contributors, but is clear and readable.

METHODS OF TREATMENT. By Logan Clendening, M.D., Clinical Professor of Medicine, Medical Department University of Kansas, and Edward H. Hashinger, A.B., M.D., Clinical Professor of Medicine Medical Department, University of Kansas; with chapters on special subjects by twelve others. Eighth Edition. St. Louis: The C. V. Mosby Company, 1943. Price $10.00.

All the methods of treatment in internal medicine are given in outline in this book. In it are collected material and details from many services, widely scattered, which helps the student or practitioner to decide what treatment to use in any given condition, and exactly how to use it. Hypodermic and intramuscular or intravenous injections are described, and complete procedures outlined. One hundred and seventy-six pages are devoted to drugs, their actions and indications, as well as methods of administration.

The article on anesthesia by Prof. Lorhan is a thorough treatise of fifty-six pages, discussing local and general, spinal and rectal anesthesia; all ten types of agents and their use and control.

Diet and infant feedings, physical methods, hydrotherapy and psychotherapy are all elaborately outlined, after which the last half of the book deals with specific disease conditions and groups. The authors discuss methods of treatment and the reasons, and specu-

late on results. This is a book of 1033 pages, well and clearly printed in good sized type, spaced for easy reading, and on non-gloss paper.

RECONSTRUCTIVE SURGERY OF THE EYELIDS. By Wendall L. Hughes, M.D., F.A.C.S., Hempstead, New York. Illustrated. St. Louis: The C. V. Mosby Company, 1943. Price $4.00.

The repair or reconstruction of the eyelids for correction of civil or war injuries is the text for this monograph written as a thesis for admission to the American Ophthalmological Society. The history of plastic surgery of the eyelids is traced with numerous illustrations of methods and results. The first chapter covers the history and development of skin grafting. Grafting without a pedicle, variations of the pedicle grafts, and general considerations regarding grafting constitute the first half of the book. Reconstruction of the conjunctiva, reconstruction of the tarsus, and transplantation of the cilia and other lid structures are well covered and illustrated. The balance of the book is a very clear exposition of the author's own method of blepharopoiesis. Cases are illustrated, and a complete reference list is given covering 451 references. The book is very well written, and nicely presented. It is worth while.

ROENTGENOGRAPHIC TECHNIQUE. A manual for physicians, students and technicians. By Darmon Artelle Rinehart, A.M., M.D., F.A.C.R. Professor of Roentgenology and applied Anatomy, School of Medicine, University of Arkansas; Roentgenologist to St. Vincent's Infirmary, Missouri Pacific Hospital, and the Arkansas Children's Hospital, Little Rock, Arkansas; Trustee, American Registry of X-Ray Technicians. Third Edition, Thoroughly Revised. 471 pages. Illustrated with 201 engravings. Philadelphia: Lea & Febiger, 1943. Price $5.50.

The third edition of a technical book is testimony of its value. This edition has allowed a thorough modernization of the text material. New techniques and new methods have been generously incorporated, and considerable new material added. The book is not too technical, bearing in mind the use by x-ray technicians, medical students, and practitioners who work for themselves and their colleagues. Emphasis is placed on the methods of developing a technique suitable to the office and conditions under which the practitioner will work, and considering his equipment. The basic principles of electricity and x-rays are given, with a thorough explanation of the tubes, instruments and office arrangement, and practices. Simple techniques are given for most of the body parts that are to be rayed, with pictures, and good descriptions. Many of the pictures are dual, one showing the position for taking the picture, and the other the x-ray obtained. The position of the tube is illustrated, with a description giving the exact details of arrangements and technique. The author advises experimentation to determine amount of exposure, and confidence in the procedure. It is a valuable guide, well printed.

THE GENEALOGY OF GYNAECOLOGY. History of the development of Gynaecology throughout the ages. 2000 B.C. —1800 A.D. With excerpts from many authors who have contributed to the various phases of the subject. By James V. Ricci, A.B., M.D. Associate Clinical Professor of Gynaecology and Obstetrics, New York Medical College, Director

of Gynaecology of the City Hospital, New York, etc. Department of Gynaecology and Obstetrics of the City Hospital, New York. Philadelphia: The Blakiston Company, 1943. Price $8.50.

This is a beautiful sample of the printer's art, a book of 578 pages, large type, easily readable. The author has done a tremendous piece of research and has presented a study of the earliest knowledge of female disease, picturing prehistoric knowledge, the Egyptian papyrus, Babylonian, Assyrian, Hindu and Biblical literature. The quotations are extensive, and each chapter is followed by a voluminous bibliography. There are seven ancient Egyptian papyri, on medical subjects, but the Kahun papyrus deals especially with gynaecology. The Griffith deciphering is given in full. The Vedas are quoted. These, with the Biblical writings antidate Hippocrates by roughly eight hundred years. The gynaecological practices down the ages are given, with comments and quotations. Two pages of twenty plates each show the vaginal speculæ used from 49 A.D. in Rome to 1821. There are fifty-four illustrations of great interest as historical studies. To the student of medical history, this book is invaluable, and to the gynaecologist with a yen for knowledge of his subject, it is a gold mine. Throughout the text there are many beautiful quotations chosen from the masters through the ages, which add charm and meaning to the gynaecological items culled from the past.

AN INTRODUCTION TO SOCIOLOGY AND SOCIAL PROBLEMS. A Textbook for Nurses. By Deborah MacLurg Jensen, R.N., B.Sc., M.A., Instructor in Sociology and Social Problems at Schools of Nursing of St. Louis City Hospital and St. Luke's Hospital; Lecturer in Nursing Education, Washington University. Illustrated. Second Edition. St. Louis. The C. V. Mosby Company, 1943. Price $3.25.

Sociology and social problems are courses of study and practice taking the efforts of many nurses who are entering special fields of work, and must have special preparation. This textbook is a systematic exposition of the subject, suitable for the nurse, but also for any individual especially concerned with sociological contacts, the doctor of medicine, and the social workers in general. The development of the family, with its various interests, contacts, and conditions from the earliest times to the present, is described. Community organizations, social problems due to divorce, maternity, sex behavior, unemployment and child welfare are discussed at length, and very sane discussions and solutions are offered. This is a worthwhile book.

THE BOY SEX OFFENDER AND HIS LATER CAREER. By Lewis J. Doshay, M.D., Ph.D., Psychiatrist Children's Courts, New York City. Formerly Senior Assistant Physician Manhattan State Hospital, New York; etc. Foreword by George W. Henry, M.D., Associate Professor of Clinical Psychiatry, Cornell University Medical College. New York: Grune & Stratton, 1943. Price $3.50.

The significance of early sex offenses in relation to later life behavior is studied in relation to 256 juvenile sexual cases treated at the New York City Children's Court Clinics and followed for a period of six years after the last treatment. The background of the delinquent, the family and home factors, personalities of the parents, age of delinquent, color, intelligence, physical disorders are all studied. Types of offenses have a bearing on future offenses. Many case histories are

given illustrating successes and failures. This is the first study so far attempted on this subject. From statistical analyses and the case histories there is evidence that adult general offenses stand in direct continuity with juvenile general offenses. On the other hand, it is patent that juvenile offenses *per se,* do not mar the personality of the individual, nor condition him to later general antisocial behavior. The whole study is very interesting. Many preventive suggestions are made, and tables given.

COLLECTED PAPERS OF THE MAYO CLINIC AND THE MAYO FOUNDATION. Edited by Richard M. Hewitt, B.A., M.A., M.D.; A. B. Nevling, M.D.; John R. Miner, B.A., Sc.D.; James R. Eckman, A.B.; and M. Katharine Smith, B.A. Volume XXXIV—1942. 999 pages with 176 illustrations. Philadelphia and London: W. B. Saunders Company, 1943. Price $11.00.

The 1942 edition of the collected papers of the Mayo Clinic is volume thirty-four, and is fully up to the high standard set so many years ago. Five hundred and thirteen papers are used to make up this volume; one hundred and thirty-seven from the staff meetings of the clinic, and others appearing in various places. This year two are copied from THE JOURNAL of the Michigan State Medical Society. These papers cover every field of the practice of medicine, and are grouped in their presentation. Recent advances in chemotherapy, the alimentary tract, genito-urinary organs, ductless glands, blood and circulatory organs, skin and syphilis, head, trunk and extremities, chest, brain, spinal cord and nerves, radiology and physical medicine, anesthesia and gas therapy gives one a comprehension of the scope of the collection. There is also a miscellaneous section. Seventy-seven of these papers are complete. The type is large, clear, and the paper not too glossy for easy reading.

INJURIES OF THE SKULL, BRAIN AND SPINAL CORD. Neuro-psychiatric, Surgical and Medico-legal Aspects. By Samuel Brock, M.D., New York University. Second edition. Baltimore: The Williams and Wilkins Company, 1943. Price $7.00.

This is a new, enlarged edition of a well-known and most useful text, written by twenty-three specialists in this field. A most comprehensive volume, this book will serve the specialist as well as the practitioner who cannot find consultant experts in the present-day physician shortage on the home front.

All degrees of head injuries are covered in detail. The work on acute and chronic subdural hematoma is particularly good. Operative technique is dealt with in a most understanding manner. The mortality of gunshot wounds of the brain has been cut from 50-60 to 28.5 per cent in the present war, using sulfanilamide powder (the choice of the sulfonamides) and azochloramide irrigation. Observations from Pearl Harbor head wounds reveal less unconsciousness due to the increased velocity of missiles now used. Vitallium and ticonium plates have been added to the list of preferred materials for skull defects.

Acute effects of cerebral birth injuries and their sequelæ account for at least one-third of the deaths within the first two weeks of life. The use of electroencephalography in diagnosis and in estimation of the

prognosis of posttraumatic convulsive and allied states is discussed.

Neuroses, malingering, roentgenological aspects of skull injuries, general pathological considerations in injuries of the spinal cord and the medico-legal aspects of injuries of the skull, brain and spinal cord are taken up in detail. The industrial surgeon will find this a necessary addition to his library.

MANUAL OF FRACTURES. TREATMENT OF EXTERNAL SKELETAL FIXATION. By C. M. Shaar, M.D., F.A.C.S. Captain, Medical Corps, United States Navy, and Frank P. Kreuz, Jr., M.D., F.A.C.S. Lieutenant Commander, Medical Corps, United States Navy. Philadelphia: W. B. Saunders and Co. Price $3.00.

This book gives a comprehensive and detailed description of the Stader reduction and fixation splint, its mechanical principles and its application to specific fractures. While advocating the Stader splint, the general principles set forth and the sites for insertion of the pins are applicable to other types of external skeletal fixation. Meticulous attention to detail is essential to the successful use of this valuable addition to the methods of treating fractures. This manual should be found helpful to all who are interested in this new technique.

PICTORIAL HANDBOOK OF FRACTURE TREATMENT. By Edward L. Compere, M.D., F.A.C.S. Associate Professor of Surgery, Northwestern University Medical School; Chairman, Department of Orthopedic Surgery, Wesley Memorial Hospital; Consulting Orthopedic Surgeon, Chicago Memorial Hospital; and by Sam W. Banks, M.D. Associate in Surgery, Northwestern University Medical School; Attending Orthopedic Surgeon, Chicago Memorial Hospital. Chicago: The Year Book Publishers, 1943.

Written for the general practitioner, medical student or intern, this book gives in compact but adequate form the treatment for the more common injuries encountered in practice. The authors have avoided presentation of several different methods of management for each type of injury, but have given the simplest principles and methods which in their hands have given uniformly satisfactory results. The book is well illustrated and should prove a handy, ready reference for the busy practitioner. The chapter on compound and infected fractures is condensed but comprehensive.

for the management of constipation

Habit Time for Bowel Movement in convalescence is decidedly a valuable factor which contributes to the patient's well-being and comfort.

A weakened system, recovering from the ravages of disease, must be aided gently and persistently in the restoration and ultimate maintenance of physiological activity.

After years of professional use, Petrogalar stands established as a reliable, efficacious aid for the establishment of comfortable bowel action.

Petrogalar Laboratories, Inc.
8134 McCormick Blvd. Chicago, Illinois

Petrogalar
REG. U.S. PAT. OFF.

Constant uniformity assures palatability —normal fecal consistency. Five types of Petrogalar provide convenient variability for individual needs.

Petrogalar is an aqueous suspension of pure mineral oil each 100 cc. of which contains 65 cc. pure mineral oil suspended in an aqueous jelly.

DR. MARGARET BELL
701 S. FOREST AVE.
ANN ARBOR, MICH. MJ